TROPICAL MEDICINE

JACKSON

TROPICAL MEDICINE

WITH SPECIAL REFERENCE TO

THE WEST INDIES, CENTRAL AMERICA, HAWAII AND THE PHILIPPINES

INCLUDING A GENERAL CONSIDERATION OF TROPICAL HYGIENE

BY

THOMAS W. JACKSON, M. D.

LECTURER ON TROPICAL MEDICINE, JEFFERSON MEDICAL COLLEGE, PHILADELPHIA.
MEMBER OF THE AMERICAN SOCIETY OF TROPICAL MEDICINE. LATELY
CAPTAIN AND ASSISTANT SURGEON, UNITED STATES VOLUNTEERS.

ONE HUNDRED AND SIX ILLUSTRATIONS

PHILADELPHIA
P. BLAKISTON'S SON & CO.
1012 WALNUT STREET
1907

422

Printed by
The Maple Press.
York, Pa.

PREFACE.

In deference to a time honored institution, a few prefatory lines may be proper and they will also afford the writer a desired opportunity to express his thanks to those who have made lighter the compilation and creation of this book.

The purposes, scope and plan of the work are set forth in the Introduction.

Each day the claims of Tropical Medicine upon American interest are more freely admitted by the medical profession and although we have no established school for the exclusive training of men in tropical pathology and hygiene, as yet, the necessity for such an institution is widely conceded and doubtless will be properly met in due time. Certain of the larger medical colleges have already established lectureships and courses of instruction for senior and advanced students and it is pleasant to think that the men who now go forth from these institutions, some of them to practice our profession in the extended tropical possessions of the United States, will have a conception of exotic diseases and pathology, which will guide them into paths of useful and satisfying work.

Great problems of investigation and administration are to be solved and Americans are confronted by obligation and opportunity. Without volition on our part, we have become responsible for the government and education of millions of men and women in distant parts of the world, who differ from us in race, traditions and civilization. Without doubt the most important part of this work of education is that touching the physical well-being of these people. Very decidedly, we are the "keepers" of our brethren, black, brown, yellow and white.

If we accept the duty of teaching these people how to live and how to maintain health, prosperity and happiness, we must have an understanding of the principles and doctrines we seek to impart to others. If this book contributes in any degree to this understanding the writer will be gratified.

If I failed to acknowledge my indebtedness to the works and writings of the English experts in Tropical Medicine I should be uncivil and unfair. In order to present a comprehensive view of some of the diseases considered, it has been necessary to quote extensively from their writings. In such cases, however, I have endeavored to give proper credit, throughout the book, and I have placed at the end of the volume a list of references consulted.

To that pioneer, path-finder and life-long worker in tropical diseases, Sir Patrick Manson, I desire to make particular acknowledgment. Without access to his writings the preparation of this book would have been difficult, indeed.

In the few instances where my experience has led me to views differing from those held by acknowledged authorities, I have endeavored to make apparent the fact that my views are personal ones, and I desire them to be accepted or rejected, by the student, after confirmation or after failure to verify them.

For cheerful encouragement during many days of my tropical residence, some of them made dreary by poor health, I recall, thankfully, the fellowship of a comrade now departed, and for encouraging interest in the labor of writing and preparation, I acknowledge gratefully the assistance of my devoted wife, Louise O. Jackson.

The publishers, P. Blakiston's Son and Company, have placed many facilities at my hand for furthering my work and have shown a friendly interest which is appreciated.

My thanks are due to Major Walter D. McCaw, United States Army, Librarian of the Surgeon-General's Library at Washington and formerly Lecturer on Tropical Medicine at the Jefferson Medical College, Philadelphia, for courtesies shown to me at various times and also to Major Charles F. Mason, United States Army, for valuable criticisms and suggestions made during the progress of the preparation of this volume.

To all others who have aided me by counsel, interest, or in any manner, I extend my thanks and I trust that this book will serve the purpose for which it has been prepared.

Philadelphia, Pa.,
December, 1906.

CONTENTS.

PART III.

Diseases of Undetermined or Uncertain Causation (Local and Constitutional), and Skin Diseases.

TROPICAL MEDICINE.

INTRODUCTION AND A GENERAL CONSIDERATION OF TROPICAL HYGIENE.

In the preparation of this work upon Diseases of the American Tropics, meaning thereby the southern portion of the United States, Cuba, Porto Rico and the Pacific Islands which float the American flag, viz.:—The Hawaiian and Philippine Islands and Guam, a definite purpose has been kept constantly in mind and two paramount ideas have been accorded first consideration.

This purpose has been to prepare for American medical men and students a simple and systematic presentation of the known and determined facts concerning such Tropical Diseases as are found within the boundaries of our own territory. Scarcely seven years have passed since the United States acquired, almost simultaneously, extensive tropical possessions in both the Eastern and Western Hemispheres. Previous to this time, naturally enough, Tropical Diseases did not strongly appeal to the American medical mind. Since then, however, there has been developed a lively and earnest interest, widespread and growing, in the diseases of our new possessions, not only on the part of the men whose duties in the various Departments of the Public Health Service took them personally to this medical terra incognita but also on the part of medical men at home. To this latter class there came a large number of cases of imported Tropical Disease, brought home along the new paths of commerce or by our returned soldiers. This flow of clinical material continues and will long continue. Coin-

cidentally medical workers at home have recognized and identified in certain sporadic and occasional diseases not previously well understood, maladies well known in the tropics and heretofore believed to be peculiar thereto. By way of illustration let me cite dysentery, both amebic and bacillary, and ankylostomiasis or hook-worm disease. Many cases of amebic dysentery have been encountered in the United States in individuals who have never passed beyond its boundaries. The much dreaded infantile scourge, cholera infantum, which annually swells so greatly the midsummer infant mortality in our great cities has been definitely proved to be identical with the bacillary dysentery of the tropics. Ankylostomiasis (hook-worm disease) and other parasitic intestinal diseases long believed to be peculiar to warm countries are now known to be endemic here, not only in Texas and other Southern states but also in latitudes much farther north.

The threatening possibilities of the importation of such diseases as bubonic plague and Asiatic cholera, which are so frequently endemic or epidemic in tropic countries, are neither fanciful nor imaginary, and this truth is recognized by many medical men.

These facts seem to justify me in my purpose. At present I am unaware of any similar American work. European writers, notably the British and Germans, have dealt with Tropical Diseases as they occur in their own respective national possessions and the best works extant are from their pens, but they have not, to any great degree at least, invaded our American tropics.

Fortunately the past seven years has witnessed such an accumulation of valuable data by American medical observers, particularly Army, Navy and Marine Hospital officers, that the task of compilation, classification and presentation is made possible and reasonably easy. This mass of information exists largely in the form of government and individual records, monographs, medical journal articles and the reports of various commissions organized for the investigation of Tropical Diseases. The material has the merit of being modern and scientific and unusually free from the mysticisms and traditions which cumber medical literature generally. Many of the investigations deal with phases of disease as yet

undetermined, and it is the writer's purpose to avoid the discussion of these undetermined questions to as large an extent as possible. Wherever facts seem to be scientifically established they will be stated as facts. Other sources of information used in this work include the writer's personal experience in Cuba and the Philippines and the British and German writings above referred to. A list of references will be found appended.

The paramount and guiding ideas which have determined the size, scope, and character of this book are Utility and Simplicity. The former consideration, Utility, has governed me in omitting from consideration, other than simple mention or reference, a number of Tropical Diseases which either have not been observed in the American tropics or which occur so rarely as to be almost never encountered by the army, navy or marine hospital surgeon or by the civilian medical observer. For those who are interested in these rarer Tropical Diseases the larger and more exhaustive European treatises are recommended.

The second consideration, that of Simplicity, has been applied in the treatment of nomenclature and of bacteriology and parasitology. The desirability of simplicity in nosology is universally conceded and needs no championing. Unfortunately many inappropriate and misleading names are so firmly established by long and almost universal use that they cannot be superceded at once by descriptive terms. This is especially true of Tropical Diseases. Numerous diseases, which we have every reason to believe widely prevalent in the tropics, have been given the names of the cities, towns or countries in which they have been observed. Thus geographical names have been prefixed to such terms as fever, sickness, sore, boil, ulcer, bubo, etc., resulting in extreme confusion. This practice has as little justification as the prefixing of personal proper names to the term disease. Both practices should be discouraged in the interests of a simple and scientific nomenclature.

Under **bacteriology** and **parasitology,** wherever a simple method of laboratory procedure is known to give satisfactory results, it *alone* is described. It is not deemed wise to discourage

laboratory diagnosis by detailing numerous or complicated procedures where a simple and single one would suffice. Comparatively few men realize how few and simple are the methods and articles of equipment absolutely essential to laboratory diagnosis (see Appendix). The microscope, of course, is absolutely indispensable for effective work, but except for this somewhat expensive instrument the essential articles are few and inexpensive and it is often possible to improvise them. Fortunately the government medical officer is very liberally supplied with laboratory instruments, apparatus and guides, so that even in the field he can usually apply the microscopic test in his diagnostic investigation. The civic practitioner, if he be a city dweller, can almost always secure access to an equipped laboratory and the country practitioner with a microscope and an intelligent understanding of principles can accomplish a great deal.

In classifying the diseases we are to consider I have attempted to group them into the following divisions: (I) Systemic Infections (chiefly bacterial in origin). (II) Diseases due to Animal Parasites. (III) Diseases of Undetermined or Uncertain Causation (local and constitutional), and Skin Diseases.

In the first group, Systemic Infections, have been included two diseases which might with propriety be classed with the second group. Both amebic dysentery and malarial disease are well known to be caused solely by animal parasites, entameba dysenteriæ and hemameba malariæ respectively, but usage and convenience warrant us in classifying them with the systemic infections, and indeed malarial disease might properly be placed in either class.

There is such a lack of unanimity in the views of various observers concerning the identity of the condition or group of symptoms usually designated as Sprue, Psilosis or Tropical Aphthæ that I have not seen fit to include it in the list of Tropical Diseases. I have, however, referred to the condition and described it in the chapter upon Dysentery. All of the cases diagnosed as psilosis, sprue or tropical aphthæ which I encountered in the Philippines might be clinically regarded, it seemed to me, as phases of chronic

gastro-intestinal catarrh plus stomatitis, or as atrophic changes in the entire digestive mucous membrane, secondary to chronic gastro-enteritis or dysentery, i.e. a degenerative process. Several observers so regard it but others maintain that the condition is really a distinct and well-marked disease and it is so considered in certain works on tropical diseases. Up to this time there has been no conclusive evidence adduced to show that the condition has a specific bacterial cause or that it is due to any animal parasite which inhabits the alimentary tract.

In view of these facts and my own personal impressions, as well as the recorded postmortem findings, I have omitted it from the classified list of diseases.

PERSONAL HYGIENE.

This is not a treatise upon hygiene and sanitation but there are a few considerations of personal hygiene that are of immense importance in connection with the prophylaxis of disease in the tropics. These may be briefly dealt with here in a general way and specifically referred to under the head of prophylaxis in the individual chapters. Every medical man in the tropics owes it to himself and to his family to supervise and to closely scrutinize all the details of his surroundings, environment and daily habit of life, regardless of any sanitary or hygienic supervision that may be undertaken for the community by civil, municipal or military authorities. If each individual had the requisite intelligence, knowledge, disposition and means to carry out the simple laws of personal hygiene the problem of maintaining health in the tropics would be greatly simplified.

The measures that safeguard the individual from most of the diseases of the tropics may be divided into two great classes: I. Measures for the Maintenance of Good Tone of Digestion, Blood, Skin, Muscles and Nervous System by Nonmedicinal Agents. II. Measures of Protection Against Infection.

In the first class of measures are included (a) cleanliness, (b) appropriate and nourishing foods, (c) appropriate clothing and

provision for its sanitary washing, (d) exercise, (e) rest, and (f) avoidance of excessive heat and exhaustion.

(a) PERSONAL CLEANLINESS.

Cleanliness of the person is secured by the generous use of clean water and soap. Owing to the increased activity of the sweat glands in warm climates the body bath becomes a daily necessity. Bathing by immersion is not always possible on account of scarcity of water and lack of facilities and when it is possible should not be performed in stagnant or muddy pools or sluggish streams, but rather in rapidly moving water. Soap is an indispensable adjunct to any bath taken for purposes of cleanliness. The shower bath has much to recommend it, particularly if taken in rain water. A daily supply of rain water is readily obtained during at least four months of the year and the dangers of skin infections, which are present in pools and bathing places frequented by natives and animals, are absent. A discarded five-gallon kerosene tin, (in which style of container this commodity is usually shipped to the tropics), may be perforated and placed on a shelf arranged six or eight feet from the floor and the bather may stand upon a wooden or bamboo rack raised a few inches from the ground. This apparatus may be readily improvised and one or more refreshing baths taken each day upon rising, retiring, or when putting on clean linen. In the absence of rain water the shower bath should be taken in water from a source known to be fresh and pure and uncontaminated by natives or animals. Otherwise it should be boiled and cooled. The possibility of acquiring disease from the application of contaminated water to the skin is not a fanciful idea, particularly in the tropics.

(b) APPROPRIATE AND NOURISHING FOOD.

In considering the matter of appropriate and nourishing foods we must take into account experience and common sense as well as a knowledge of the physio-chemistry of digestion, assimilation, and heat production. These matters are thoroughly dealt with

in the standard works on Hygiene and will not be considered here. My personal experience convinces me that the health of our troops in Cuba, and particularly in the Philippines, was maintained rather than injured by the liberal dietary supplied, although the government ration furnished was loudly condemned by a few persistent writers as being far too rich in fat and heat producing elements. Experience also demonstrated that native (Malay) troops whose customary diet of fish, rice, and similar foods was augmented by the issue of articles of the United States army ration, rapidly improved in appearance, strength, effectiveness and the ability to withstand disease.

I recall very distinctly one striking case of inanition which occurred in an American school teacher in the Philippines.

This gentleman was an athletic, college-bred young man of about twenty-five years, who was placed in charge of a native school in a town about thirty miles from Manila. He was intelligent and well informed as to the dangers of infection and the methods of prevention but was so situated as to be unable to secure with ease the articles of diet to which he was accustomed. He was likewise imbued with the idea that the food products of the United States were inappropriate for the tropics and he adopted the native diet cheerfully, even though from necessity. At the same time he took daily exercise very energetically and methodically to the point of fatigue. At the end of some weeks he consulted me professionally for loss of strength, mental and bodily energy, and failing weight, but presented no evidence of organic or functional disease. After careful investigation of his case I concluded that the condition was entirely due to a lack of nutritious food and I prescribed a liberal diet, including meats and wheat products, and assisted him in arranging to secure the needed articles. The return of health and vigor was almost magical and permanent.

Speaking in very general terms the Summer time diet of the United States would not be inappropriate in any of the American tropics. Two of the essential food products, fresh meat and milk, are often difficult to procure, but eggs are usually obtainable.

(c) APPROPRIATE CLOTHING AND PROVISION FOR ITS SANITARY WASHING.

We will consider the matter of appropriate clothing for the tropics from the view-point of the civilian. In all branches of the military service the uniform, (usually an appropriate one), is prescribed by the authorities, upon the recommendation of boards of officers which have made extended studies and observations of the special conditions and needs of the soldier. These special conditions do not always apply to the civilian, however. Matters to be taken into account in this connection are material, weight, color and absorbing power. Clothing for the body and extremities will be considered separately. The American or European will usually be most comfortable with two sets of garments, an inner set worn next to the skin, and an outer set. Undergarments should be made of materials which are light in weight, absorbent, non-conducting as to heat and nonirritating. No one fabric material, perhaps, combines these qualities perfectly. Silk, woolen, linen and cotton materials are commended by various authorities. Silk, while nonirritating to a high degree, easily becomes saturated with perspiration, in which state it is heat conducting. It is also expensive. Wool is irritating to most skins and shrinks when boiled or washed in hot water. Linen absorbs excellently and dries quickly, while cotton is less absorbent and dries less quickly. Neither linen nor cotton possesses the warmth of silk or wool, a quality which most authorities insist upon as essential, the chilling of the abdomen after excessive perspiration being considered a fruitful cause of gastro-enteric disorders. A mixture of wool and silk constitutes an excellent combination, particularly for protection to the abdomen, but it is expensive also and unless extremely light in weight is rather too warm for comfort. Linen and cotton undergarments can be worn with more comfort and with safety, except at night when warmer garments should be put on. The abdomen, at least, should be protected by a warmer fabric. Pajamas, the shirt of which should be long and tucked within the drawers, are the most satisfactory sleeping garments. It is highly important that the underclothing material be porous,

absorbent, not easily saturated, nonirritating and susceptible of boiling without injury to the fabric. The color should be light. The outer garments should be light in weight and color, loose fitting and washable. An excellent material is the twilled goods known as khaki cloth, obtainable in either white or brown. It is strong, does not require starching and is not injured by hot water. Starched goods are uncomfortable, unsanitary and when saturated with perspiration, unsightly. Shirts should be of the soft bosom variety. The head gear should be light in color, amply ventilated, generous in shading qualities and featherweight. The sweat band should be separated from the inner surface of the hat, by a space of a quarter inch or more, by means of cork connections placed far apart. If helmet shaped, there may be generous side openings in the dome for ventilation. The brim should be broad and so extended as to protect the neck and base of the brain from heat as well as sunburn. The Indian pith helmet or hat, white in color, is probably the best tropical head gear although straw hats properly constructed are useful. The ventilated "campaign" hat of the army also has its advocates. The problem of foot gear requires special consideration also. Stockings should be of cotton and light in color. If leather shoes must be worn they should be as porous at it is possible to get them and tan in color. If one's occupation will permit, low Oxford ties of tan leather may be worn, but low shoes have a disadvantage in that they do not protect the ankles, favorite points of attack for mosquitos. In view of this fact they should not be worn at night or where mosquitos are troublesome. The most comfortable shoe, according to my experience, is the soft white canvas laced shoe extending above the ankle and provided with a moderately thin leather sole. This shoe permits of excellent ventilation but has disadvantages in rainy weather. It can be worn with comfort and benefit at other times, however, and can be scrubbed and kept presentable by applications of "Blanco" or pipe clay.

There has been considerable discussion, pro and con, of the possibility of contracting "dhobie" or washerwoman's itch through the medium of clothing, and while most observers agree that the

washing of garments without heat or boiling,(the usual practice of native washerwomen in all hot countries) is a possible source of tricophyton infection (ring-worm) they consider the danger a remote one. It has been contended that drying garments in the tropical sun minimizes the danger, but from personal observation and experience I am convinced that the native method of washing clothes, or the handling of them by native washerwomen is productive of a very large percent. of the body ring-worm infections, at least in the Philippine Islands. I have also observed that the institution of reforms in washing methods in garrisons has reduced the incidence of the disease in a most striking manner. In view of this observation and the conceded fact that other and graver skin affections, and even systemic infections, may be transmitted in clothing, I should be recreant if I failed to insist upon the disinfection of clothing, either by immersion in disinfectant solutions during the washing process or by subjecting the clothing to boiling when washed. The latter method is the preferable one and if observed will protect the dweller in a tropical country from almost certain infection, sooner or later. It is difficult and well-nigh impossible to persuade the native laundress of the necessity for boiling clothes and unless the proceeding is supervised it is reasonably certain that your injunctions will be disregarded.

The safest and most satisfactory plan is to have the washing and ironing done at one's own quarters, providing a good sized vessel for boiling the clothes, and personally seeing that instructions are carried out. If clothing is sent out of the house it will almost certainly be washed in some filthy stream, pool or public washing place, and conveyed to and fro in baskets which are probably infected with germs or vermin. In cities it is possible, of course, to have the washing done in steam laundries, a reasonably safe arrangement.

In his recent book entitled "Effects of Tropical Light on White Men," (1905) Major Woodruff, United States Army, advises the wearing of dark (black or yellow) undergarments if white outer clothing is worn, in order to intercept the *light* rays which are freely transmitted by white clothing and which have been blamed

for many of the skin and nervous affections of blondes in the tropics. Speaking of this combination of white outer garments and black underclothing he compares it with Nature's protective provision for certain animals which have white hair and black skins. "It reflects most of the heat and light and allows few actinic rays to penetrate, and experience proves the combination to be very comfortable." Woodruff insists that clothing and head gear be *opaque* and states that the color is immaterial so long as it does not transmit the shorter light waves and the infraviolet. He advises white, gray, or yellow for outer clothing for those exposed to direct rays of the sun. In the helmet a dark lining or an inner layer of dark material serves to intercept the objectionable light rays. He also objects vigorously to certain tropical habits of house building and house lighting (by daylight) on the same score. He advises the darkening of houses, the building of porches in such a manner that the sky will not be visible to persons seated upon them, the prohibition of white houses in cities, the painting of buildings green, brown and dark yellow and the exclusion of excessive light from hospitals and houses, attributing many cases of malaise, neurasthenic headache and neuralgia, particularly in blondes, to tropical light.

(d) EXERCISE.

Exercise is as important and essential to the preservation of health in the tropics as it is in temperate climates, but the amount, variety and the times of day at which it should be taken are important considerations. It is manifestly impossible to formulate any rules applicable alike to all persons. The personal equation must always be dealt with as temperamental and physical differences in individuals directly affect and modify their needs in this matter. There can be no doubt that exercise has a value, aside from its effect upon the physical well-being of the body, for purposes of diversion and the averting of nostalgia. Homesickness undoubtedly has a direct inhibiting effect upon the ability of the individual to withstand disease and is a powerful depressant of

the vital forces. To be healthful, then, exercise should be of such a character as to divert. It should never be taken during the heated portion of the day nor to the point of exhaustion. The most appropriate times for exercise are the early morning and the late afternoon hours. In the morning it will be well to take moderately brisk exercise after a very light meal, between the hours of seven o'clock and nine o'clock, varying from half an hour to an hour and a half in duration, according to the activity of the exercise taken. In the evening a similar period of time may be devoted to exercise just before sunset and preceding the evening meal. Among the best varieties of exercise are horse-back-riding, walking, tennis, quoits and rowing.

Calisthenic exercise, or "setting-up" drills such as practised by soldiers, are excellent also. Never to pursue any form of exercise to the point of exhaustion is a golden rule. A bath (not necessarily a cold one) and a change of clothing should follow the exercise, especially the morning installment.

(e) REST.

In the matter of rest the same considerations as to time and kind must be taken heed of. The term, as used here, includes not only sleep but cessation from work of every kind. The total amount of sleep required by an adult in the tropics varies but little from the amount required by the same individual in a temperate country. The distribution of hours may differ somewhat but the total number of hours taken will be about the same. Earlier rising will about compensate for midday sleeping, as a rule. The daily hours of labor, either physical or mental, should never exceed eight and as a general rule the same amount should be devoted to sleeping. The remaining eight hours will be divided between eating, which should be done deliberately, dressing and bathing, exercise and passive recreation, such as conversing, driving, card-playing, music or light reading. The tropic visitor will soon discover that the early morning hours just after sunrise are the most pleasant of the day, and he should reform any habits of

lying abed in the morning to which he may have been addicted at home. He will also find that the midday hours are entirely unsuitable for labor of any kind and will do well to be guided by the native population in the matter of midday resting, To the average American the setting aside of three or four hours for rest (from noon till 3 or 4 p. m.) seems at first an extravagant waste of time, but in this view he is entirely in error and if he properly values his health and is wise, he will not insist upon the arduous routine of life observed in cooler lands.

The siesta or afternoon rest should invariably be taken reclining and it is much better to disrobe and to go to bed, whether one sleeps or not.

(f) AVOIDANCE OF EXCESSIVE HEAT AND EXHAUSTION.

The necessity for avoiding fatigue has already been mentioned in connection with (d) Exercise and (e) Rest and the necessity for avoiding the midday heat and direct sun rays has also been mentioned. Aside from the general effects of excessive heat and fatigue in the tropics, in lowering vitality and lessening resistance to infections, there may be mentioned the danger of insolation (sunstroke), the discomforts of "prickly heat" (a condition of acute inflammation of the sweat glands following excessive activity of perspiration), and the discomforts and dangers of sunburn, which not infrequently causes extensive skin destruction and invites pus infections. Preventive measures are chiefly included under the topics we have just been considering: Appropriate food, clothing, rest, exercise, cool drinks, bathing and the avoidance of exposure.

II. MEASURES OF PROTECTION AGAINST INFECTION.

These measures include the exclusion of infection (a) by Water, (b) by Food, (c) by Clothing, (d) by Contagion and (e) by Bites of Insects and Vermin.

(a) BY WATER.

Mention has already been made of the possibility of acquiring disease by means of water externally applied and the measure of prevention has been given. At least one serious animal parasitic infection, (ankylostomiasis), is frequently acquired through the skin and it is doubtless true that other parasites whose habitat is frequently mud and water may and do find entrance to the body through lesions in the integument; hence the importance of uncontaminated water for bathing.

An American woman while traveling in the Southern Philippines fell from a bridge, sustaining a compound fracture of the leg, which in falling was covered with mud and water. Antiseptic dressing was immediately made by an American surgeon of the party but the bacillus of malignant edema had gained entrance, and prompt high amputation of the thigh alone saved her life.

As might be expected, tetanus bacillus infection is quite common in the Philippines.

Other possible routes of infection by water are through the rectum and vagina. One can easily understand the dangers of introducing water containing amebas of dysentery or spirilla of cholera into the body, by means of vaginal douches or rectal enemata, in countries where these diseases prevail, unless care be taken to use only sterile water for injection purposes. These practices are common among Americans and Europeans in the tropics, as well as elsewhere, to secure personal cleanliness and to overcome rectal obstipation.

The teeth should never be brushed except with sterile water.

A far greater danger, however, lies in the *ingestion* of water contaminated by bacterial and animal parasitic organisms, with which tropical waters teem, the sustained warm temperature assuring one of the conditions for culture and multiplication absent in temperate or cold countries. In this fact lies one of the great causes for the wide distribution and prevalence of disease in warm countries.

We know to a certainty that a number of the most prevalent and deadly diseases of the tropics are water borne and practically

always contracted through the medium of ingested water. The danger is so obvious that one would expect intelligent white persons, cognizant of the facts, to adopt, thankfully and instantly, the simple and effective preventive measures offered. But such unfortunately is not the case and will not be so long as human nature remains perverse. Only those who have served with troops supplied with sterile and absolutely safe drinking water can realize that men will violate regulations, even upon pain of punishment, and seek and drink polluted water from pools and streams in preference to that known to be pure, wholesome and health preserving. Only in the presence of an epidemic of cholera, such as we experienced in the Philippines, was it possible to secure absolute observance of orders in the matter of drinking water, and in this case the penalty of disobedience was so swift and fatal as to impress the soldiers with the horrors of the fate which followed infraction of the law. The most eloquent commentary on the observance of the rule forbidding the use of unsterilized water was the immunity enjoyed by our troops, while all about us the natives beyond our control died like sheep.

Dysentery, typhoid fever, cholera, hook-worm disease, and intestinal worms are among the infections usually communicated by drinking water.

The remedial measure may be stated in a few words.

Destruction of the bacteria, animal parasites and ova which infest water, by *boiling*, renders the water safely potable.

The resultant brew does not, however, appeal to esthetic tastes, on account of the presence of the dead bacteria and other organisms, but filtration, previous to boiling, mechanically removes the vast majority of all germs present, large and small, and so minimizes this objection. The dwellers on steamships (as in our navy and transport service) enjoy a marked advantage in being furnished distilled water at all times and in all parts of the world. Water boiled after filtering, preserved and dispensed in sterilized containers, is an admirable substitute, and may be said truthfully to be the most potent agent for the prevention of disease, in the tropics, known to man. The details of preparation should never

be entrusted to an unskilled or irresponsible person, for a failure in the technique of cleanliness and sterilization may vitiate the entire proceeding and put into jeopardy the lives of many people.

During the American occupation of Cuba and the Philippines the Medical Department of the Army carefully considered the subject of water sterilization in its practical phases, and in December, 1898, a board of medical officers was appointed to determine upon the best method of furnishing sterilized water for troops in the field. After exhaustive tests and experiments with numerous devices submitted for trial the board reported, in August, 1889, in favor of the apparatus known as the Waterhouse-Forbes Water Sterilizer, a portable device of about 150 pounds weight, capable of delivering 300 gallons of sterilized water every twelve hours (a supply for two companies), aerated and cooled to a temperature less than five degrees above the temperature of the water as it enters the sterilizer. The sterilization is effected by boiling and the heat is applied by means of an oil burner, which is operated at an expense of about four cents an hour. The heat given up by the boiled water is applied to elevating the temperature of the incoming, unsterilized water in the pipes, before it reaches the point where the direct heat of the oil burner causes sterilization. Tests showed that all germs except a few spore-bearing bacteria were destroyed, and that typhoid bacilli and colon bacilli were completely destroyed. When the sterilization was preceded by filtration the quality of water was excellent and perfectly safe.

Having personally observed the operation of the apparatus, and also used its output of sterilized water, both in Cuba and the Philippines, depending upon it in the midst of a cholera epidemic, I can unhesitatingly subscribe to its usefulness, especially if preliminary filtration be had. The annual report of the Surgeon-General of the Army for 1901 states that: "In the Philippines the Waterhouse-Forbes sterilizers are in use throughout the Islands and give the utmost satisfaction, although care in their management must be taken to insure a thorough sterilization." The report for 1902 states that: "Chemical sterilization of water has hardly been attempted (in the Philippines), all purification methods

depending upon heat applied in different ways. A great deal of distilled water is furnished by Medical Department ice plants, and by distilling plants belonging to the Quartermaster's Department, much water is boiled, and a considerable amount obtained from Forbes-Waterhouse sterilizers."

A portable water still, made in convenient sizes, which has been furnished to some army stations in the United States for hospital or laboratory purposes, is the Ralston New Process Water Still which is pictured in the appendix.

(b) BY FOOD.

When food acts as the carrier of infection it does so in one of several ways. The germ of disease may either be contained within the food itself (as in the case of parasites in the cystoidal state in meats) or they may be deposited upon the surface of foods, such as fruits, vegetables, salads, meats, rice, etc., either by man, in handling, or by insects, such as flies. Flies may also deposit their eggs upon foodstuffs and the larvæ may be hatched within or upon them. After the deposition of bacteria, if the foodstuff be a good medium for cultivation, the organisms may multiply within it or upon the surface and their virulence may be enhanced by their cultivation.

Pathogenic organisms may also gain entrance to prepared foods through the water used in mixing or diluting the ingredients. Milk, soups and gelatin foods offer themselves as particularly good culture media and should consequently be handled and protected from exposure with the greatest care.

Oysters are particularly dangerous in the tropics both as ptomaine producers and as bacteria carriers.

Examples of conveyance of infection by food are familiar enough and it will be sufficient to mention some of the diseases thus conveyed. Amebic dysentery, acute infectious dysentery, typhoid fever, cholera, tape-worm, hook-worm and other intestinal parasitic diseases, are among the number and there are probably others among the diseases whose etiology is at present obscure.

The preventive measures to be taken are sterilization, cleanliness in handling, protection of food from flies and animals, avoidance of raw foods raised in the ground (where manure has possibly been used for fertilizing), the avoidance of oysters and similar shell fish uncooked and the avoidance in general of all raw foods not above suspicion. Most fruits and vegetables with thick or dense skins may be disinfected by scalding them, shortly before eating, without injuring their qualities. Vinegar is destructive to cholera spirilla and probably to other bacteria of weak resistance but I should not advise dependence upon it for disinfection under any circumstances. Cooking affords the most efficient disinfection and sterilization of foodstuffs attainable.

Putrefaction and decay should always be guarded against and their occurrence of course absolutely condemns the foods so affected. Tropic conditions are so favorable to putrefactive change that one is only safe in using strictly fresh products.

(c) BY CLOTHING.

The principal points in connection with the avoidance of infection by clothing have been detailed under the heading (c) Appropriate clothing and provision for sanitary washing. In that section the possibility of acquiring disease through clothing and the preventive measures were set forth and need not be repeated here.

(d) BY CONTAGION.

As here used, contagion means contact of the body, either with actually diseased surfaces (as in syphilis) or with the infected atmospheric zone which immediately surrounds the bodies of persons with such few contagious diseases as are known to be thus communicable through air zones; or contact of the body with soil, bedding, floors, walls, etc., containing pathogenic bacteria or animal parasites within or upon them. An example of such contagion would be the acquiring of tetanus through contact of the bare feet with soil containing the bacillus of this disease. It is probable that a broken

skin or some lesion of the integument is a necessary condition for contagion of this variety. The preventive measures include avoidance of such contact, protective inoculation when possible (as vaccination in smallpox), protection by occlusive antiseptic dressings of all lesions of the skin, the wearing of stockings and shoes and the disinfection of infected surfaces, bedding and soil whenever known to exist.

(e) BY BITES OF INSECTS AND VERMIN.

The avoidance of bites of insects and vermin, as a measure of protection from infections, has assumed very great importance during the past few years. The list of diseases known to be communicable only through the bites of insects is small, and doubtless incomplete, but it already embraces two of the most deadly and dreaded diseases of the tropics, malarial fever and yellow fever. Flies undoubtedly act as carriers of disease-producing bacteria, such as typhoid and cholera bacilli, and certain biting flies convey trypanosomes, parasitic blood organisms which are pathogenic to man as well as animals. Rats have been shown, repeatedly, to be capable of acquiring, harboring and transmitting disease, notably bubonic plague, but whether or not they are able to inoculate man through the medium of their bites is an undetermined question. I have known, personally, of numerous instances in the tropics of these rodents biting and wounding sleeping men and children, however, and it is certainly a matter for serious investigation, particularly in view of the fact that a large number of the rats captured and bacteriologically examined in Manila, Hong Kong and other tropical cities, have been shown to be infected with plague bacilli, many of them dying from plague. Our knowledge of the whole subject of disease-producing insects and vermin is very incomplete, however, and all that is definitely known will be found under appropriace headings in the chapters devoted to the various diseases, in the causation of which insects and vermin are implicated, and in the brief discussion of mosquitos to follow.

The bites and stings of snakes, scorpions, tarantulas, centipedes and venomous creatures generally and of ticks, leeches, chiggers (sand fleas), screw worms and burrowing insects, are not here referred to as infectious. The lesions produced by the non-venomous insects are local but may be followed by suppurative processes as dependent upon infection by pyogenic bacteria. The systemic effects of bites from venomous creatures resemble toxemias and chemical or alkaloidal poisoning rather than bacterial infectious diseases. In Africa and Persia fevers following the bites of certain ticks have been reported as "tick fevers" but in the tropical insular possessions of the United States such maladies, if encountered, are rare at least and generally unrecognized. Venomous serpents are likewise comparatively rare in our tropical possessions and no where do the conditions approach those of India where thousands die annually from the bites of venomous snakes. The snakes of Cuba and the Philippines are generally harmless although some specimens of great size are found (boas and rock pythons). Those of the Southern United States, rattlesnakes, copper heads and moccasin snakes, are far more dangerous than the snakes of the Philippines and Cuba. The following paragraph is quoted from the annual report of the Surgeon-General of the Army for 1905: "Notwithstanding that a large part of the army was serving in the tropics there was no admission for snake bites."

MOSQUITOS.

The discoveries that yellow fever and malarial disease are inoculable by mosquitos have stimulated a widespread inquiry into the distribution, classification, reproduction-habits and life-history of these insects and it has likewise revolutionized quarantine methods and greatly rationalized tropical hygiene. Much of the collected data concerning mosquitos has no direct bearing upon disease conveyance and does not concern us in our study of tropic diseases. But with regard to a few common varieties our security, as well as our comfort, demands that we make warfare upon them. Within the past few years hundreds of new varieties of mosquitos

have been discovered in various parts of the world and the classification is constantly changing. Howard's book upon mosquitos of the United States, Theobald's and Giles' books upon mosquitos and gnats and Ross' "Mosquito Brigades" will afford the student of medicine ample information concerning these insects. For our purpose we may divide mosquitos into two classes, pathogenic and nonpathogenic. Fortunately the nonpathogenic class is much larger than the pathogenic. The varieties now known to be pathogenic may be included in three great divisions:

Anophelina, Culex and **Stegomyia** mosquitos.

The parasites of malaria are borne and inoculated by Anophelina mosquitos only. Yellow fever is transmitted and inoculated by Stegomyia fasciata. Filarial disease is mosquito borne, filariæ being chiefly transmitted by Culex fatigans although a certain Anopheles mosquito may also convey these blood parasites. It is desirable, therefore, that the practical medical man shall be able to distinguish between these varieties of mosquitos and shall know their habits of breeding, feeding, and biting and their life-histories, even though he may not possess an intimate knowledge of the entire mosquito family.

The following statements, abstracted largely from the writings of Ross, Howard, Manson, and Giles, apply to mosquitos of all varieties and are facts which should be known by medical men and all others interested in public health and sanitation.

Mosquitos and gnats are identical, the latter term being little used in America.

"All mosquitos breed in stagnant water."

Mosquito larvæ must live in water at least six days before wings are developed. If either larvæ or eggs are exposed to drying they die.

When the adult (winged) insect stage is attained, individuals may live for months, hibernating in cold weather and resisting frost or severe heat. They feed upon leaves, fruit, birds, animals and man, the females only feeding upon blood.

"It is now a matter of the general experience of many investigators that where mosquitos abound in the house their larvæ can usually

be found at a short distance, say within a few hundred yards from the house. Occasionally where the house is isolated and no stagnant water is in the immediate vicinity, mosquitos may attack it from a greater distance; but this is exceptional and

Fig. 1.—Mosquito Eggs of Several Varieties. *a, b.* Culex; *c.* Egg-raft or boat, Culex; *d.* Stegomyia; *e.* Anopheles showing escaping larvæ. (Beyer.)

in the great majority of cases, especially in towns, almost every house breeds its own mosquitos in its back yards, or in puddles and drains in the streets close by."

The development process of the mosquito, from egg to winged

insect, is an interesting one requiring from ten days to a month, according to species and conditions, the process being accelerated or retarded by favorable or unfavorable conditions, viz., warmth or cold. Conditions being equal the development period for Culex mosquitos is shorter than that for Anopheles insects. The impregnated female mosquito deposits her eggs upon the surface of still water where they float until larvæ hatch from the eggs. These wriggling larvæ breathe air and spend most of the time at the surface of the water. The larva feeds upon the organic matter in the water and after days of growth, during which it moults (casts its larval skin) several times, the pupa stage is attained. It now becomes less active, ceases to feed and remains chiefly at the surface of the water. In a few days the pupa case bursts and the winged mosquito stands upon the floating shell until its wings are dry and then takes flight.

Observations by Howard showed the development period for Culex specimens under favorable conditions to be ten days and that for Anopheles species in cooler weather to be twenty-four days. The duration of the various stages, egg, larval and pupal, varies greatly according to conditions.

As has been stated, a vast number of species of mosquitos, grouped in a number of genera, exist. The two commonest groups embrace all the disease-carrying mosquitos known at present. They are Culex and Anophelina mosquitos.

A recent subdivision of the Culex mosquitos into two divisions, Culex and Stegomyia, has been made but some writers continue to use the term Culex in the old sense, including Stegomyia mosquitos. In the tabulated classification of pathogenic mosquitos which I have prepared the biologic similarity and the similarity of habits of Culex and Stegomyia will be apparent. This classification with the illustrations of eggs, larvæ and adult mosquitos should be helpful, but it must be remembered that some of the distinctions made are not absolute nor invariable, particularly in the matters of breeding-places and resting positions. They represent, however, the consensus of opinion of a majority of observers.

	Culex.	Stegomyia.	Anophelina.
Breeds.	In and about houses, gardens, back yards, old flower pots, or tins, vessels, tubs, cisterns, barrels, gutters, drains. "Home bred."	Resembles Culex.	Puddle breeding—shallow, small pools, in rock or soil, also at margins of lakes and rivers, quiet bays, ponds, in rice fields and water covering submerged grass. Less "home bred."
Bites.	By day or night—at twilight. Females only.	Often bites by day. Females only.	Nocturnal chiefly. Females only.
Wings.	Rarely spotted.	Never spotted.	Usually spotted. There are a few exceptions.
Larval Motility.	Larvæ float with heads downward. When disturbed wriggle to bottom of vessel.	Resemble Culex.	Float at surface of water like sticks and have a backward, skating motion.
Resting Posture.	"Hunch backed." Axis of head and proboscis forms an obtuse angle with body.	Resembles Culex.	Axis of head, proboscis and body in same line. Appears as if standing on its head. Some exceptions to this rule.
Eggs.	Deposited in ellipse-shaped masses, convex below, concave above (boat shaped). Eggs arranged in rows, perpendicular and adherent. have one pointed end. Color dirty white. 200 to 400 in a batch.	Eggs are more oval and are not deposited in rafts or masses. Float singly upon their sides, or sink, hatching submerged.	Deposited in masses of 40 to 100 eggs, not adherent, each egg floating on its side, and regularly elliptic in outline, at middle of each side appears a clasping wrinkled membrane. Dark in color.
Singing Tone.	High pitched.	Resembles Culex.	Low pitched.
Bodies.	Dull gray in color.	Body and legs covered with black scales and white markings in spots or lines. S. Fasciata has transverse striations on ventral aspect of body.	Dark gray or brown.
Diseases Conveyed.	Mostly nonpathogenic for man but may convey filarial diseases.	Stegomyia fasciata conveys yellow fever in man.	Conveys malarial disease. Conveys filarial disease in man.

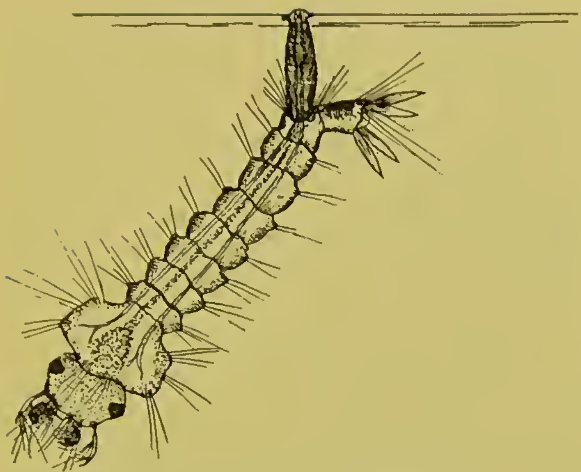


Fig. 2.—Culex Larva. (Beyer.)

Fig. 3.—Culex Pupa or Nymph. (Beyer.)

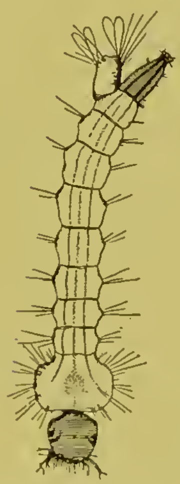


Fig. 4.—Stegomyia Larva. (Beyer.)

Fig. 5.—Stegomyia Pupa or Nymph. (Beyer.)

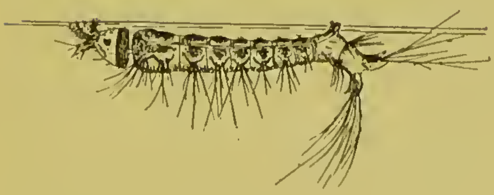


Fig. 6.—Anopheles Larva. (Beyer.)

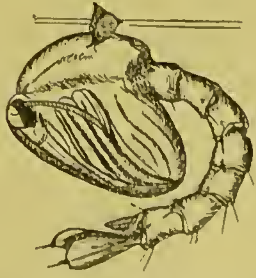


Fig. 7.—Anopheles Pupa or Nymph. (Beyer.)

In "Climate and Health in Warm Countries" (p 102) Colonel Giles of the Indian Medical Service (retired) writes as follows: "For our purposes it will suffice for the reader to understand the general characteristic of these sorts of mosquitos. First, there are the common Culex mosquitos, which are, almost everywhere, far more common than the others. They are usually of a dull gray color, and with very few exceptions, their wings are quite plain and free from spots. . . . They sit in rather a humped up position, and the proboscis is obviously much thinner than the body, its appendages, or palps, being held apart from it. Mosquitos of this sort cannot convey human malaria though they are instrumental in conveying a similar disease for certain animals. They are to be found, in greater or less numbers, throughout the year.

"The second sort is the Stegomyia, which is the genus concerned in the conveyance of yellow fever. These mosquitos rest in much the same position as Culices, which they resemble closely in form. Their wings are never spotted, and almost all are small insects clothed with jetty black scales, picked out with an ornamentation of dazzling white lines on the body and spots on the abdomen and legs.

"The third, or Anopheles, subfamily is that concerned in the transmission of human malaria, and . . . can easily be recognized by their characteristic form and attitude. In these mosquitos the feelers are long and thick in both sexes, and as they are held habitually in contact with the proboscis, they appear to the naked eye as a prolongation of the body as thick, or thicker than the abdomen. Moreover, except in a few species, their position, when resting, forms a singular contrast to that of the Culices, the whole body and proboscis being held in one straight line, with the abdomen raised from, and the proboscis pointed almost vertically at the surface on which they rest, and almost touching it with the point, as if they were preparing to drive the latter into it; so that viewed with the naked eye, they look like minute black thorns stuck into the surface on which they are sitting. On closer examination it will be seen that the wings are not plain

Fig. 8.—Culex Tæniorhynchus, Wiedem (female).
(From "The Spread of Disease by Insects," by Major C. F. Mason, U. S. A. International Clinics, 1904, by kind permission.)

but spotted (the number of plain winged species being unimportant)."

To summarize briefly, the Culex mosquito is "home bred," laying its eggs in and about houses, barrels, gutters, drains, flower pots and similar places. It bites both day and night but most at twilight, the female mosquito only feeding on blood. Its eggs are deposited on the water in boat-shaped masses containing from 200 to 400 eggs, which are arranged in rows, the eggs perpendicular and adherent, each with a pointed end. The color is a dirty white. The wings of the mosquito are plain and but rarely spotted. The larvæ float, heads downward, and wriggle to the bottom when the water is disturbed. The color of the

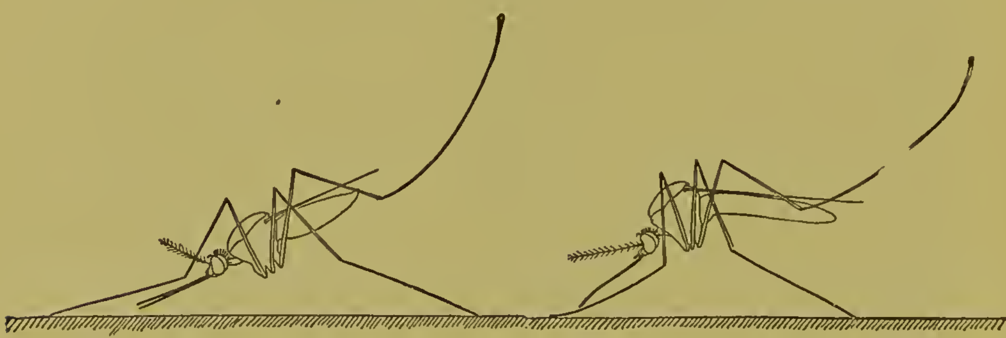


Fig. 9.—Anopheles. Fig. 10.—Culex.
Resting positions of Anopheles and Culex insects. (Drawn by C. O. Waterhouse.)

Culex insect is dull gray and the singing note is high pitched. In the resting position they are hunch-backed, the axis of body and head and proboscis forming an angle. This variety is the most common one and this insect cannot convey any disease organisms to man (so far as known) except certain filarial blood parasites.

The Stegomyia mosquito was considered a sub-variety of the Culex family until recently. It resembles Culex in its selection of breeding-places, in its singing tone, its resting position and its plain unspotted wings. The female mosquito often bites by day and does not lay her eggs on the water in masses or rafts. They float singly upon their sides or sink, often hatching under water.

Fig. 11.—Stegomyia fasciata, Fabr. (female)
(From "The Spread of Disease by Insects," by Major C. F. Mason, U. S. A.
International Clinics, 1904, by kind permission.)

The body and legs of this mosquito are covered with black scales and marked by white spots or lines. A variety of this genus, Stegomyia fasciata, conveys yellow fever from man to man.

The Anophelina group comprises many varieties, at least twenty of which have been proved to be bearers of malaria parasites. The Anopheles insect is "puddle-breeding" and less house-bred than the genera just described. In her biting habits the female is chiefly nocturnal. The wings are with few exceptions spotted. She lays her dark colored eggs in masses of 40 to 100. These eggs are not adherent, each egg floating upon its side in the water. It is regularly elliptic in outline. At the middle of each side a wrinkled, clasping membrane appears. The eggs hatch at the surface of the water and the larvæ float like sticks and have a backward, skating motion. At rest, the insect appears somewhat as if standing upon its head, the axes of body, head and proboscis being about in the same line. Its singing tone is low pitched and its color dark gray. It conveys malaria parasites from man to man and may also carry filarial disease.

To differentiate mosquitos a strong hand glass or a low power microscope lens will be needed, an inch objective serving nicely. The mosquitos should be killed quickly by vapor; chloroform, cyanide or tobacco smoke answering the purpose. They may then be preserved in alcohol or mounted at once. Alcohol renders them friable and does not permit satisfactory dissection, if this is desired. Mosquitos may be mounted in Canada balsam or glycerine jelly, on a slide with a cupped depression, and sealed with a cover-glass, or they may be examined directly beneath the objective. If preserved the specimens should be carefully labeled. Examination of mosquito eggs will prove quite as useful for beginners as the examination of the insect itself. We cannot take up the subject of mosquito dissection in this work, nor can we consider the destruction of mosquitos, except to emphasize its importance and to mention a few principles.

To destroy mosquitos we must attack them in the water during their larval and pupal stages, or in the air as adult insects. We may also destroy their breeding-places by ditching, drainage,

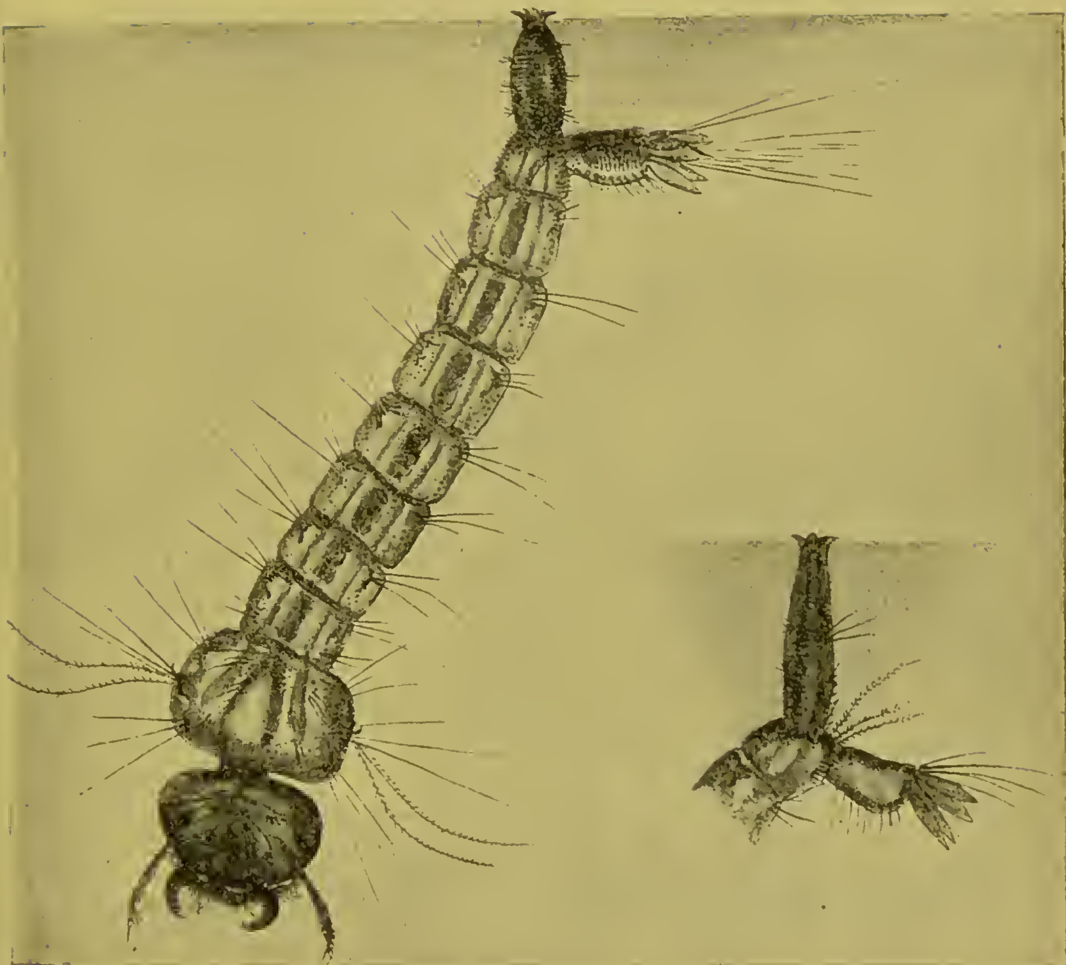


Fig. 12.—Mature larva of Stegomyia fasciata. To the right, for comparison, respiratory siphon of Culex.

(From "The Spread of Disease by Insects," by Major C. F. Mason, U. S. A. International Clinics, 1904, by kind permission.)

or by leveling them. The destruction of breeding-places is the more rational procedure but when dealing with immense areas, as we sometimes must, the problem becomes one for sanitary engineers and financiers. The method of destroying the insect is only practicable during the larval and pupal stages, that is during the aquatic existence of the mosquito. Having once taken flight from his pupal shell and become a creature of the air the mosquito is, to a very great degree, beyond the reach of our destructive endeavors, although we may attack him within the confining limits of a room, or a house, by creating a toxic atmosphere for him. When we attack the insects in the water, however, we destroy armies instead of individuals.

Kerosene (mineral oil), by virtue of its property of spreading in a thin film over large surfaces of water, has proved to be the most valuable agent thus far proposed. It is, practically, always to be had and is inexpensive, the cheaper grades being perfectly satisfactory for the purpose. A gallon will cover a surface of water equivalent to 3000 square yards, within two days, with a film so thin as to be absolutely safe from fire but entirely larvacidal. A renewal of the film every two weeks will suffice in water that is stagnant or very slowly moving. For the technique and details of mosquito destruction the student is referred to Giles' works on "Gnats" and "Climate and Health in Warm Countries," Ross' "Mosquito Brigades" and to various authorities upon sanitary engineering.

Trypanosomes, peculiar blood parasites which infest the blood of certain animals and man, in the tropics, are conveyed in all probability, through the bites of flies. Whether or not the varieties of trypanosomes which produce nagana or surra in animals and "sleeping-sickness" in man are essentially identical or closely related is a problem still undetermined, but it is more than probable that certain horse-flies or cattle-flies act as intermediary hosts and convey the organisms of these diseases, through their bites, either to man or to animals. These flies, generally speaking, are "hard-shelled" which fact renders them resistant to injury and less likely to be killed. The entire subject of trypanosomiasis is still in its

Fig. 13.—Anopheles Maculipennis, Meigen.
(From "The Spread of Disease by Insects," by Major C. F. Mason, U. S. A. International Clinics, 1904, by kind permission.)

infancy. The studies leading to the present beliefs concerning its dissemination by biting flies have all taken place within a few years and the results up to this time are incomplete.

Comparative Tables Showing Temperature, Humidity, and Rainfall Monthly and Annually for the Cities of Havana, Cuba, and Manila, P. I., and New Orleans, U. S. A. Compiled from Tables in Giles' "Outlines of Tropical Climatology." Rainfall in Inches. Temperatures in Fahrenheit.

Havana, Cuba, Lat. 23° 9′ N. Long. 82° 23′ W.—Sea Level.

Month.	Mean Temperature.	Maximum.	Minimum.	Relative Humidity.	Rainfall (inches).	Number Rainy Days
January	70.3	84.4	52.3	75	2.71	7.5
February	72	87.6	51.4	73	2.27	5.7
March	73.2	91.4	55	70	1.83	5.5
April	76.1	93.6	52.9	69	2.83	4.6
May	78.8	99	64.4	71	4.47	9.3
June	81.5	97.7	69.1	76	7.16	12.8
July	82.4	100.6	71.2	74	5.06	12.7
August	82.2	98.6	69.8	75	6.02	12.6
September . . .	80.7	96.1	70.9	79	6.71	15.4
October	78.1	91.9	61.9	78	7.42	15.1
November . . .	75.3	88.7	56.5	77	3.08	10.2
December . . .	71.4	86	51.8	74	2.15	8.5
Year.	76.3 Average.	100.6	51.4	74 Average.	51.73 Total.	119.9 Total.

Manila, Lat. 14° 36′ N. Long. 120° 58′ E.—Sea Level.

Month.	Mean Temperature.	Maximum.	Minimum.	Relative Humidity.	Mean Rainfall (inches).
January	77	93	62.1	77.7	1.19
February	77.7	95.7	61	74.1	0.41
March	80.4	95.9	63.3	71.7	0.74
April	82.9	99	66	70.9	1.14
May	83.3	100	71.1	76.9	4.20
June	82	97	70.9	81.5	9.62
July	80.8	94.8	70	84.9	14.57
August	80.8	94.3	69.1	84.4	13.87
September . . .	80.4	93.7	70.5	85.6	14.93
October	80.4	94.8	68.7	82.6	7.54
November . . .	79	92.1	64.9	81.6	5.13
December . . .	77.4	91.9	60.3	80.7	2.13
Year.	77 Average.	100	60.3	79.3 Average.	75.46 Total.

New Orleans, Lat. 29° 58′ N. Long. 90° 11′ W.

Month.	Mean Temperature.	Maximum.	Minimum.	Relative Humidity.	Mean Rainfall (inches)	Number of Rainy Days
January	58.8	82	15	79	5.17	11
February	58.1	82	25	81	4.56	10
March	62	84	30	76	5.35	9
April	69	88	38	76	5.28	8
May	74.6	92	53	74	4.76	9
June	80.3	97	58	78	6.49	14
July	82.2	99	67	78	6.50	16
August	81.5	96	63	79	6.02	14
September	78.3	95	56	77	4 70	11
October	69.8	90	40	74	3.25	7
November	60.7	85	30	79	4.30	9
December	55.5	81	20	80	4.38	4
Year.	68.8 Average.	99	15	78 Average.	60.52 Total.	128 Total.

Rainfall and Temperature in Honolulu, Hawaii, and Colon, Panama.

Honolulu, Lat. 21° 18′ N.

Warmest Month, Aug., Mean Temperature 77.5° F.
Coldest Month, Jan., Mean Temperature 69.5° F. } Difference 8.5° F.

Month.	Rainfall (inches).
January	4.03
February	4.58
March	3.77
April	3.14
May	3.16
June	1.82
July	2.53
August	2.28
September	1.85
October	2.28
November	5.16
December	4.93
Year.	39.45

Colon, Panama. } Lat. 9° 22′ N. Long. 79° 55′ W.

Warmest Month, June, Mean Temperature 79.8° F.
Coldest Month, Nov., Mean Temperature 78.5° F. } Difference 1.3° F.

Absolute Mean Maximum 94.3° F.
Absolute Mean Minimum 66° F.

Month.	Rainfall (inches).
January	1.88
February	1.49
March	1.30
April	2.65
May	11.40
June	13.67
July	14.4
August	14.64
September	12.40
October	13.54
November	23.18
December	11.98
Year.	122.37

PART I.

SYSTEMIC DISEASES.

(Chiefly Bacterial in Origin.)

CHAPTER I.

CHOLERA.

Synonyms. Asiatic Cholera; Cholera Infectiosa.

Definition. Cholera is an acute, infectious, epidemic disease, due to the presence in the intestine of a specific vibrio, or spirillum (Koch's comma bacillus). It is clinically characterized by frequent and profuse dejections and vomiting of a colorless, serous material, resembling rice water, by agonizing muscle cramps, by suppression of urine, great wasting of the fluids and tissues of the body, an algid state with rapid collapse, and by a very high mortality.

Facts of Geography and History. Although this disease is doubtless one of great antiquity, reliable records concerning it date back only to the early part of the nineteenth century, when it first invaded Europe as an epidemic, in 1830. For thirteen years preceding this invasion the disease had spread over the continent and islands of Asia, from the Pacific Ocean to the Mediterranean and Caspian Seas, starting from Southern India, where for centuries it has been, and is now, endemic. From Russia, where it first appeared in Europe in 1830, it spread south and west, over the continent of Europe, the British Isles and across the Atlantic into the United States and Canada, reaching our country in the summer of 1832.

This European pandemic lasted several years. In the United States, in 1832, the disease extended west to the Mississippi river and gradually abated, disappearing with the onset of winter. It appeared again in 1835-36 and in 1848 reappeared in New Orleans, thence spreading northward and westward to the middle states and the Pacific Coast. It again appeared in the United States in 1849, '54, '66, '67 and '73 in brief epidemics, although prevalent in Europe in epidemic form, at brief intervals, from 1840 to 1895.

During the great Hamburg epidemic, in 1893, a few cases reached New York but the disease did not gain a footing upon our soil.

From a study of epidemics Manson (Tropical Diseases, p. 345) points out "that cholera reaches Europe by three distinct routes: I via. Afghanistan, Persia, the Caspian Sea and the Volga Valley; II via. The Persian Gulf, Syria, Asia Minor, Turkey in Europe and the Mediterranean; and III via. The Red Sea, Egypt, and the Mediterranean."

There can be no doubt whatever that cholera, perhaps more than any other disease, travels and extends along the paths of commerce and that the comparative isolation of numerous spots and localities which escape visitations of cholera during epidemics, explains, to a great degree, their immunity, although there are striking exceptions to this rule, not always readily explained. During the great Hamburg epidemic certain parts of the city were practically free from its ravages while adjacent portions were devastated. In this case, however, the explanation was a simple one, the immune portions of the city receiving their water supply purified by filtration, while in the infected portions river water was pumped directly into the mains.

During recent years, particularly the past five years, owing to the prevalence of cholera in China, Straits Settlement, the Philippine Islands and Japan, the western border of the United States has been seriously threatened, through and along trans-Pacific routes of travel.

Although those nations which have high regard for sanitation and maintain effective quarantine laws are most safeguarded, no country of the civilized world is exempt from the possible danger of the importation of cholera and, indeed, very few places which lie along the commercial highways and water-ways of the world have escaped its visitations. While in a sense cholera is a cosmopolitan disease and not strictly a tropical one, it has its home in tropic countries and works its greatest depredations there. Nearly if not quite all of the countries to which this book specially relates have been visited by epidemic cholera, one or more times, during the last fifty years.

Etiology and Prophylaxis. Concerning the cause of cholera we have definite and fairly complete knowledge and it may be stated positively that the disease is caused solely by the spirillum commonly known as Koch's comma bacillus.

In 1883 Robert Koch discovered this organism and established its causal relation to cholera. Sent to Egypt by the German government, at the head of a commission of expert pathologists, during an epidemic of cholera in 1883, he shortly announced to his government the discovery in the stools and intestines of cholera patients, of a peculiar organism, not present in other circumstances, which he and his conferes believed

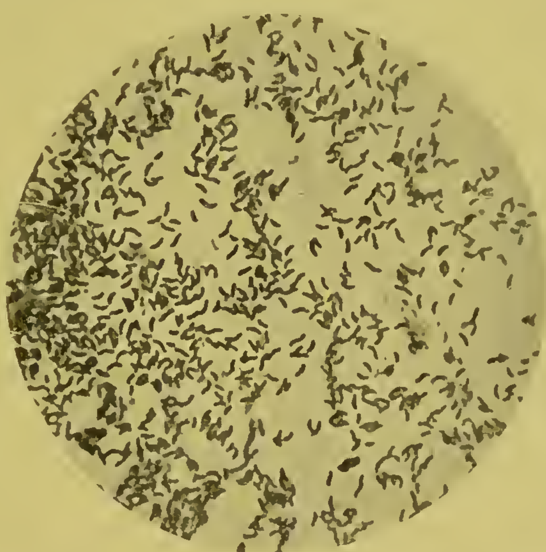


Fig. 14.—Spirillum of Cholera. (x 1000.) After Williams.

to be the specific causative organism of cholera. The Egyptian epidemic died and his government sent Robert Koch to India to further confirm and establish his findings, which he finally did to the satisfaction of the scientific world in the face of bitter and violent opposition on the part of rival scientists engaged in a similar search.

For fifty years prior to Koch's announcement the cause of cholera had been the subject of continuous and fruitless investigation, from the time that Malgaigne visited Warsaw, in 1832,

to study the new plague which had appeared in Europe but two years before. It is neither necessary nor desirable to detail the experimentation which led to the discovery and its subsequent acceptance by scientists from nearly every country in the civilized world, and a summary of the facts relating to the morphology, cultural characteristics, recognition, method of distribution and diagnostic import of the cholera spirillum only, will be set forth here.

The spirillum measures from one to two microns in length and about one-third of a micron in breadth and grows outside of the body upon various media, such as gelatine agar-agar, peptone bouillon, potato and blood serum, some of which it liquefies. It grows with or without oxygen but more rapidly in its presence and most characteristically upon gelatine, which it liquefies. Growth and liquefaction in stab cultures of gelatine begin at the surface and extend downward along the puncture line, the growth taking a funnel shape and usually showing an apparent bubble of air (an optical illusion) in its expanded portion.

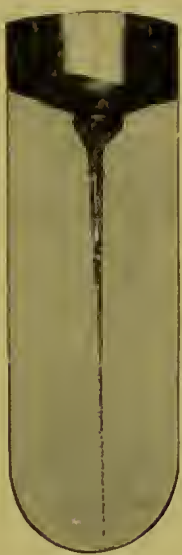


Fig. 15.—Spirillum of Cholera, stab culture in gelatine, two days old. (Fränkel and Pfeiffer.)

On plates of gelatine round, white points appear in twenty-four hours, or less, and later the growth takes on a granular or furrowed appearance, viewed under a low power glass. Liquefaction takes place and the colonies drop into the cupped depression so caused, growing there in central, irregular masses. As liquefaction of the medium goes on the growth loses its characteristic appearance.

The spirillum is possessed of great motility and in culture arranges itself in U and S forms (end to end), although in films direct from the intestine the long axes of the spirilla are parallel and this arrangement suggests "fish swimming in slowly moving water" (Koch's observation).

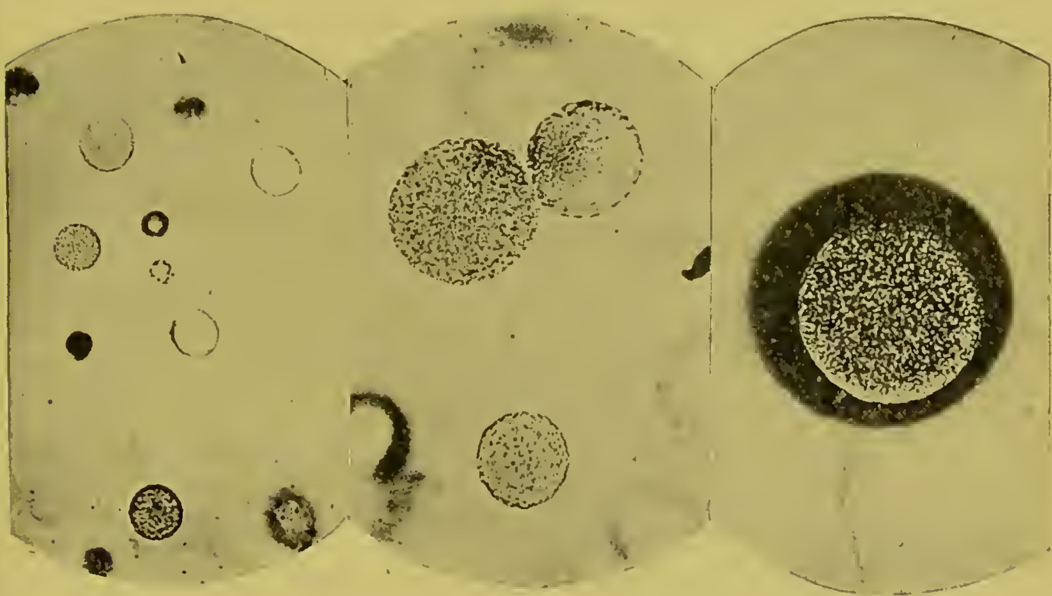
The cholera organism is reproduced by fission and develops one or two flagella (usually but one) from its poles. It grows at

temperatures between 14° C. and 42° C. but best at 37° C. (body temperature).

When introduced into the stomachs of guinea pigs, cholera spirilla produce the disease in these animals, providing an alkaline gastric condition is first secured.

Cholera spirilla stain well and easily with fuchsin, methyl blue and other basic aniline dyes and they decolorize by Gram's iodine method.

They multiply with exceptional rapidity in alkaline media and



a *b* *c*

Fig. 16.—Spirillum of Cholera, colonies on gelatine plates, (x 100 to 150.) *a*. Twenty-four hours old. *b*. Thirty hours old. *c*. Forty-eight hours old. (Fränkel and Pfeiffer.)

this rapidity of growth is a point of differentiation between them and certain spirilla which resemble cholera organisms. In alkaline bouillon, turbidity and a surface growth may be obtained in a twelve-hour culture at body temperature, a valuable point in determining doubtful cases in the early days of an epidemic. The cholera-red reaction (an indol color reaction) is obtained by the addition of a few drops of sulphuric acid (C.P.) to a twenty-four-hour pure culture of cholera spirilla in peptone bouillon. A color reaction, ranging from rose pink to red, is never absent in

cases of the cholera organism although observed in the presence of a few other bacteria. It is a valuable confirmatory test.

There undoubtedly exists an antagonism between cholera spirilla and other micro-organisms. In culture with other bacteria, in most fluids, growth of the spirilla is at first increased but later inhibited and they finally die. In the water of sewers they live but do not increase, while in distilled water they succumb after a few weeks, unless pabulum in the form of organic matter is supplied to them. Warmth, oxygen, alkalinity and organic matter favor their growth and these facts explain why cholera spirilla persist and multiply in water, fresh or salt, outside of the human body.

The acidity of the normal gastric juice, in man, is perhaps his greatest protection and one of the greatest natural prophylactic conditions. The resistance of cholera spirilla to heat and cold, to drying, to acids and to weak solutions of antiseptic agents is feeble.

Cholera spirilla gain entrance into the human alimentary tract, in the vast majority of cases, through the ingestion of water or of food contaminated with infected water. This contamination may also be borne by flies, or other insects, which convey the bacteria upon their feet, wings or mandibles directly from the exposed stools or vomitus of cholera cases, to exposed food, solid or liquid, such as rice, vegetables, meat, milk, etc. Cholera spirilla have been recovered from flies twenty-four hours after contact with choleraic stools. Fruits grown upon trees are rarely contaminated except by handling, but vegetables and salads grown in the soil may have been fertilized by human excreta (a practice in vogue among the Chinese truck gardeners of Manila previous to American supervision). The washing of raw food products in weak acid solutions has been shown to destroy cholera spirilla but it is manifestly tempting Providence to depend upon such methods in the presence of this disease.

Having stated the methods of conveyance and infection, the measures of prevention naturally suggest themselves. The only absolutely safe rule of conduct is to introduce no food into the mouth or stomach except such as has been cooked immediately before eating, and to drink no water (or milk) which has not

been distilled or boiled, and protected from infection by careless handling or storing in unsterile containers. Drinking vessels, dishes and eating utensils should be washed only in boiling water and wiped with sterile drying towels, or, preferably, dried by heat. All foods should be screened from flies, handled only with clean hands and placed only upon clean tables and dishes, which are likewise to be screened when not in use. Especial attention should be given to ice boxes and water coolers for while cold of sufficient degree destroys cholera spirilla this degree is not reached in the domestic ice box or water cooler.

Attention to these details should be consistent, unremittent and religious. If every particle of vomit or dejected matter, from every case of cholera, could be disinfected new cases would not occur; but this is plainly an ideal condition, never to be realized. Nevertheless it is our duty to strive unceasingly to bring the condition to pass.

In the meantime we must recognize actual conditions and apply the measures of prevention stated above and also any others which may suggest themselves. Public sanitation and quarantine are proper functions of government and are the most effective measures for the prevention and abolition of epidemic cholera. These most important subjects come within the scope of works upon hygiene and cannot be considered in detail here.

It will not be inappropriate for me to sketch briefly the recent epidemic of cholera in the Philippine Islands which I witnessed in 1902, and in the suppression of which I was privileged to take part. The disease appeared first in Manila, March 20, 1902, and was doubtless imported from some Chinese port, probably Hong-kong, where cholera was epidemic at the time. Between this port and Manila there was considerable commerce and Chinamen were arriving almost daily, although subjected to strict quarantine regulations. It was not until March 5, 1902, that the importation of Chinese vegetables was interdicted and after this date large quantities were thrown overboard from ships in the bay and were doubtless picked up on the bay shore at Manila by native Filipinos. It is presumed that the disease

entered Manila in this way. At any rate it first appeared in a district of the city adjacent to the bay shore and spread thence throughout Manila and later through Luzon and the southern islands, following as usual, the paths of commerce.

In most cases these paths were water routes. The entire number of cases which occurred in the archipelago during 1902–1903 has been conservatively estimated at 150,000 and the death rate approximated seventy-five percent.

The disease was chiefly confined to the native population, although Americans and Europeans did not entirely escape. The water supply of Manila, piped from the Maraquina valley, was probably never infected but the Pasig river and the numerous canals and estuaries which traverse the city of Manila, and upon which hundreds of boat dwellers had their abodes in cascoes and lorchas, were thoroughly contaminated. The disease wrought its greatest havoc, however, outside of the city of Manila and upon certain isolated small islands the population was more than decimated. A vigorous campaign of education was instituted and carried on, and the people, everywhere, were apprised of the dangers of using unboiled water. Ignorance and superstition are not to be annihilated in a day, however, and in spite of edicts, the expenditure of large sums of money for sanitation and quarantine, and highly intelligent efforts on the part of officials, the disease spread to the more remote islands of the archipelago and exacted the mortality mentioned above. The army escaped to a notable degree and many communities where government medical officers were stationed were almost entirely preserved from the disease. At the first appearance of the epidemic the civil government co-operated with the military medical authorities and all army medical officers were constituted heads of municipal health boards, and clothed with authority to enforce sanitation and the observance of sanitary laws. Considering the ignorance, superstition and poverty of the people and the social and sanitary conditions generally, the results obtained were creditable to the American authorities in the Philippine Islands, civil and military.

Cholera first appeared at my station some thirty miles from Manila, about a month after its outbreak there. During this time, however, we had constructed barriers, in the form of quarantine pickets and detention camps for travelers by land, and by the inspection of all vessels and detention of the crews and passengers, under observation, for five days, for travelers by water, and we were able to intercept the infection which finally came from Manila by water. It came in the persons of a native crew of a lorcha bearing forage for the government animals. Two cases, both of them fatal after six hours' duration, occurred on this vessel during its detention at anchor in the bay. We were able to bar out the disease in this case and for three months thereafter (so long as I remained at the station) cholera gained no foothold in the two towns of which I had quarantine and sanitary supervision.

The mental impression created by my first case of cholera is still vivid. At the time of my evening visit of inspection all aboard the quarantined vessel appeared well, when mustered for inspection, but upon the following morning one of the crew was dead with evidences of cholera. With the assistance of two of the natives from the lorcha I removed the body in a small boat to a sand bar projecting from the shore within the quarantine zone, and after causing the natives to dig a grave in the sand I made an autopsy and secured specimens for microscopic examinations. The postmortem findings were typical of cholera and the body was buried in the sand.

Microscopic examination of smears and cultures confirming the diagnosis of cholera, I returned upon the following day with a private of the hospital corps, and after exposing the body, the surrounding hot sand was saturated with many gallons of kerosene and upon this was piled a large amount of firewood when the whole was ignited and the body consumed in situ.

Of the utmost interest, in connection with the subject of the prophylaxis of cholera, is the study of immunity.

Immunity is usually divided into two varieties, natural and artificial. By natural immunity is generally understood the inherent quality of the organism to withstand infection. Vol-

umes of theories and observations have been written upon the subject but the sum of our real knowledge, all of which has been gained by observation, is far from colossal. So far as cholera is concerned we may state that while it may be impossible to deny the existence of racial and individual immunity in cholera we are justified in disregarding natural immunity and in practically assuming its nonexistence.

With regard to artificial immunity, however, the case is entirely different and we are able to state definitely that it is possible to artificially produce individual protection from cholera, of a more or less temporary character. A certain individual immunity against second attacks of cholera is also conferred by an attack of the disease, according to the best scientific evidence and the weight of opinion. It is probably a temporary condition but whether it is due to the retention of bacterial products inimical to a reinvasion of the cholera spirillum, within the body, or whether the first attack exhausts the supply of some cell-manufactured principle essential to the activity of cholera toxins in the body, is purely a speculative question as yet.

The first important recorded efforts to produce artificial immunity to cholera were those of Ferran in Spain in 1885. His practices in inoculating the noninfected population, in towns affected by epidemic cholera, were most bitterly assailed by European critics, as was also his personal character, and he was repeatedly accused of charlatanry. Shakespeare, in an interesting account (pp. 711–714, Cholera in Europe and India) of his personal investigation of the methods, claims and personality of Ferran, acquits him of this charge, even though he admits having entertained a prejudicial bias against Ferran, conceived prior to his investigation, and it must be admitted that the methods of Ferran, however crude and inconclusive they were, led directly up to the subsequent investigations of Haffkine and others and established the basis upon which rests inoculative immunity as it exists and is accepted today. The method of Ferran (1885) is in most essential details the modified Haffkine method of today. Ferran inoculated his subjects with hypodermatic injections of

bouillon cultures of cholera spirrila while the hypodermatic method of Haffkine, as described by Powell (see p. 371, Tropical Diseases—Manson) is as follows:

"The whole surface of agar in a sloped tube is inoculated with the comma and cultivated for from twenty-four to thirty-six hours at a temperature of 40° C. The whole surface should then be covered with a uniform layer of growth. Sterilized water is then added to one-third of the height of the agar and the growth washed off and suspended in the water by rotating or shaking till the surface of the agar is quite clear. Half a cubic centimeter (about nine minims) is the dose for an average adult."

I have always felt that a great opportunity for testing the value of protective inoculations for cholera was lost by the American authorities in the Philippines, in the epidemic of 1902 to which I have referred. It must be admitted, however, that the manifold duties imposed upon the medical service there, the suddenness of the epidemic and the isolation of some of the localities where the disease raged most fiercely, extenuated our failure in this matter.

Personally, the only opportunity afforded me of witnessing the effects of inoculative injections for immunity were in Nagasaki, Japan, in September, 1902, where in company with about 500 unhappy mortals I spent ten days in quarantine on a pest ship, the U. S. A. Transport "Sherman." This experience was related and the Japanese method of using cholera antitoxin and toxin was well set forth in the Journal of the American Medical Association for December 2, 1902, by Mabry and Gemmill in an article entitled "Cholera Aboard the U. S. A. Transport 'Sherman.' Experiences of the Army surgeons in charge of the cholera cases, suspects and contacts disembarked in Japan for quarantine; Description of the new Japanese antitoxin and cholera vaccine."

Our experience in Nagasaki, the courtesy and consideration shown to us by the Japanese quarantine officials, the admirable system and efficiency of their methods and the insight we secured into Japanese medical science and investigation, impressed us all most profoundly, and not the least impressive thing to us as

medical officers, fresh from the combat with cholera in the Philippines, was the superior record of the Japanese in dealing with the disease.

To quote from Mabry and Gemmill (loc. cit.): "In the treatment of cholera the Japanese are using a blood serum antitoxin and for prophylaxis a toxin or 'cholera vaccine.' The blood serum antitoxin is obtained from a horse immunized to the comma baccilus in much the same manner as that practiced in the preparation of the antitoxin of diphtheria. It is also administered to patients in the same manner as that antitoxin and in doses of from 10 to 72 grams in twenty-four hours, according to the emergency of the case. The method employed in preparation of the prophylactic toxin is not that of Haffkine nor are the reactions in any particular nearly so severe. * * * The toxin is prepared as follows: So much of a pure culture of virulent comma bacilli as can be taken up on a platinum wire with a 0.25 cm. loop is added to one gram of a 0.5 percent. solution of sodium chloride; after agitation, sufficient to thoroughly distribute the bacilli, the solution is placed in a hot water bath at 60° C. for thirty minutes, then enough acidum carbolicum added to produce a 0.5 percent. solution of that reagent and the resulting preparation injected at once or preserved in corked and sealed blue glass bottles. An injection of one gram of this toxin is determined in Japanese laboratories, by the usual means, to confer after the second day decided protection, if not practical immunity, for from four to eight weeks, the symptoms in cases of cholera developing being ameliorated and the prognosis made favorable accordingly. A second injection of two grams seven days after the first and a third of three grams after twenty-one days are determined, by the same means, to confer immunity to cholera for from fifteen to twenty four months."

According to the statements of the chief medical officer of the quarantine staff at Nagasaki, there had been treated with antitoxin at the quarantine station, up to the time of the "Sherman's" arrival, thirty-one cases of cholera, all of them taken from vessels in quarantine, and of this number but one had died.

About 700 cases of cholera had occurred in Nagasaki and outlying towns with a mortality of 35 percent, including all cases. According to the statement of the Japanese official, very few who received early antitoxin treatment died. So firmly convinced of the efficiency of this treatment were the Japanese, that they stated that they expected the recovery of every cholera case (not in extremis) to whom the blood serum was properly administered. At the time of our visit the officials were somewhat hampered in their observations by a shortage of serum, the Imperial laboratories being unable to supply antitoxin as rapidly as the requisitions came in. The quarantine officials also told us of their use of the prophylactic toxin or vaccine and stated that all persons in any way exposed to cholera at the quarantine station, doctors, nurses, attendants and coolies, had received two immunizing injections and that all had escaped infection although in daily contact with the disease. The officials also narrated their experience in rendering immune the inhabitants of a small town near Nagasaki. It was first proposed to inoculate the entire population but a sufficient supply of the vaccine was not obtainable. A large number of persons were vaccinated, however, and no cases occurred among the inoculated population after the second day, although the epidemic spread and proved very fatal among the noninoculated.

We may revert to the "Sherman" epidemic. Exclusive of surgeons and attendants, 92 sick men, (62 of them suffering from chronic dysentery and gastro-enteric diseases and 30 of them from rheumatism, tuberculosis, wounds and venereal diseases) in the process of being invalided home to the United States, were landed at Nagasaki for quarantine, after fifteen days' confinement in an unsanitary and inadequate hospital aboard the ship, during which time cholera had appeared among them. All had been extraordinarily exposed to infection, by reason of crowding, the vomiting of the seasick, the frequent bowel movements of the dysenterics, the absence of sanitary water-closets, fresh air and sunlight, and by other unfavorable conditions. No official of the United States Army Medical Department was responsible in any sense for this deplorable state of affairs, but on the contrary the medical

authorities did their utmost to avert the condition. The real causes of the situation may not be discussed here.

It was my pleasure to be instrumental in effecting this transfer of the sick, from the ship to the shore, and to have charge of the matter of securing permission from the Japanese quarantine authorities to use certain buildings upon the reservation and sampans for transporting patients to the shore, and of arranging for kitchens and sanitary provisions generally, for the sick and their attendants. After persuading the Japanese authorities of the absolute necessity of removing the sick to the shore they co-operated with us in every way and made possible the expedition and comfort with which the transfer was accomplished.

Accompanying the 92 patients transferred ashore were surgeons and attendants, swelling the number to 110 souls. The first cases of cholera among the invalids occurred when we were within about forty-eight hours' sail of Nagasaki and upon our arrival four cases had developed, two of the patients had died and one was dying. Six more cases developed, within four days after transfer to the shore, showing that the infection took place in the hospital on the "Sherman."

Of the 110 men inoculated with the Japanese cholera vaccine, none contracted the disease except those infected aboard ship (in all cases invalid soldiers or attendants). Of the four cases developed aboard the "Sherman," three died (mortality 75 percent); of the six cases developed ashore, three died (mortality 50 percent). Two of these fatal cases (developed ashore) were subjects of chronic dysentery and the third was a case of chronic gastro-enteritis. All were extremely emaciated and stood large chances of dying from their original diseases before the end of the voyage to San Francisco. Of the three recoveries among the cases developed ashore, one was in fair condition (recovering from an operation for the removal of tuberculous glands), one was in good physical condition and the third was in poor condition, with chronic entero-colitis when stricken with cholera. Aside from the six cases cited, all of them infected aboard ship, none of the 110 persons developed cholera. Eighty-five of this number

received the immunizing inoculation, the remainder of the number being in such an extremely debilitated state that Surgeons Mabry and Gemmill deemed it inadvisable to subject them to the inoculation, there being no records up to this time of the effects of the vaccine upon white persons. Surgeons Mabry and Gemmill first received the inoculations themselves, before administering them to the sick. In brief, it may be stated that reactions from the inoculations were in no cases alarming. The symptoms produced were usually pain and swelling (brief) at the points of inoculation, slight elevations of temperature, looseness of the bowels, slight headache, depression, muscle soreness and occasionally muscle cramps, the reaction covering a period from 24 to 36 hours. As the conditions of contact and exposure, depression and low vitality from disease, and surroundings of the patients in the ship's hospital had been most favorable for infection, it is not unreasonable to believe that inoculations with the vaccine prevented the development of at least a few cases and we may look upon the mortality rate of fifty percent as a creditable one, considering the wretched condition of the patients, some of them mere skeletons when they received the Japanese treatment. It must be remembered also that the one patient who recovered, of the four stricken aboard ship, received the antitoxin treatment upon arrival in Nagasaki, within twenty-four hours after developing the disease.

Upon the whole it may be said that our impressions of the Japanese methods of preventive vaccination and antitoxin treatment for cholera were profound ones and tended towards conviction.

Pathology and Diagnosis. The demonstrable pathologic changes in cholera infectiosa are found in the intestine and stomach, muscles, kidneys, liver and blood and will vary according to the stage of the disease in which death has occurred. For example, the appearance of the intestine in the case of a person dying in the acute stage of cholera may be quite unlike that observed in one who has survived the acute stage and has died in the stage of reaction. When death occurs in the acute stage, the intestine and stomach will usually be found to be more or less distended with a fluid, colorless or slightly milky in appear-

ance, highly albuminous and containing minute flakes of desquamated epithelium. This fluid is largely derived from the blood, being the exuded liquor sanguinous which pours out of the paralyzed capillaries. This fluid is markedly alkaline in reaction and may contain some fecal matter and occasionally a certain amount of bile. If these matters be present the color of the intestinal contents will be darker than otherwise. It may also be somewhat frothy.

The term "rice-water" describes its appearance better, perhaps, than any other that has been suggested. As has been stated, elsewhere, this fluid may in certain cases contain a pure, or nearly pure culture of cholera spirilla and in any case cholera organisms will be present in abundance. If reaction has been established before death, bile and fecal elements will probably be present.

The color of the stomach and intestines within the body, before incision, is a pale pink, with injected areas here and there, or the pink color may be absent. The mesenteric glands may be swollen and red. Upon incision the fluid described above will flow out and disclose a congested condition of the mucosa, with spots of injection. These appearances are more pronounced in the lower part of the ileum and decidedly less in the colon. If death did not occur in the early stages the effect of the exfoliation of epithelium will be apparent in a softened condition of the mucous coat. The peritoneal cavity contains no fluid and the peritoneal surfaces are dry. The muscles are dry, unless reaction has set in before death, and the lungs are dry unless the subject survived the acute stages. The bladder is empty; the gall bladder is usually distended and the spleen is not enlarged. The liver and the venous side of the circulatory system are full of blood, dark, thick, and sticky. The kidneys contain venous blood and are congested and may show cloudy swelling, fatty degeneration and epithelial desquamation in the tubules. The nervous system, although seriously affected by the toxins of cholera, shows no distinctive changes, except that the brain presents the same dry condition observed elsewhere, due to great losses of blood serum.

In the acute stage there will appear great wasting of the tis-

sues, sunken eyes and shrunken skin and occasionally a ruptured muscle, due to the violence of contractions. Movements of the limbs also occur after death, from muscular contractions, and rigor mortis is present early. The blood changes are profound. The fluidity of the blood is greatly lessened by the outpouring of serum and in consequence the circulation is delayed and impeded to such an extent that the blood scarcely seems to flow. The condition of algidity is, in part at least, due to this decreased fluidity.

In attempting to perform venous transfusion upon patients in the collapse stage of cholera I have personally observed this viscidity of the blood. The veins upon incision were found to be filled with blood, very dark and thick, which coagulated with great rapidity.

The red corpuscles are altered and destroyed to such an extent that oxygen starvation is also present.

Leucocytosis or its absence has no diagnostic or prognostic value in cholera.

The explanation of these pathologic changes, as accepted at present, lies in the elaboration of a toxin, or toxins, by the cholera spirilla within the intestine. This ptomain or chemical alkaloid acts first upon the mucous membrane of the small intestine, irritating that structure and eventually causing desquamation. It is also absorbed from the intestine and reaches the blood, which it profoundly alters, and through it acts upon the respiratory and vaso-motor centres. The condition is actually one of toxemia. These facts explain why treatment, directed at the local intestinal condition alone, is so futile and why such success as has been achieved has been along lines of treatment directed against the toxemia.

Cholera spirilla are not recoverable from any part of the body other than the intestine and stomach and the glands lying within the walls of these organs. We, therefore, conclude that they do not enter the systemic circulation, or at least that they do not proliferate there. They are found in the epithelial layer of the mucosa and in the intestinal lumen and also in the lumina of glands communicating with the intestine.

They sometimes penetrate beyond the superficial layer of the mucosa, however, especially where there has been extensive desquamation of epithelium, and then produce quite severe inflammation of the intestine and occasionally necrosis and hemorrhage from the mucosa with the formation of pseudo-membrane.

The occurrence, in the blood serum of animals immunized to cholera, of a principle capable of agglutinating cholera spirilla in culture has been demonstrated. This serum reaction is comparable with that occurring during and after typhoid fever and acute specific infectious dysentery. Pfeiffer demonstrated by experiment that living cholera spirilla, when injected into the peritoneal cavities of immunized guinea pigs, were rapidly disintegrated, while no other bacteria injected into the immune animals underwent this bacteriolysis. He also suggests the use of this reaction for diagnostic purposes but up to the present time no practical use has been made of it. This brings us to the subject of DIAGNOSIS.

Much that has been said under the subtopics of etiology and pathology has a direct bearing upon the diagnosis of cholera. The bacteriological method of diagnosis appears in the section on laboratory detection, at the close of this chapter, and includes recovery of the cholera spirillum from choleraic stools and its identification by culture upon various media and by the cholera-red test. The technique of these procedures will be found in detail there.

The direct and differential diagnosis by symptoms sometimes presents difficulties. There are a few diseases and conditions in which the onset and symptoms are decidedly like those of cholera, and sporadic cases of *cholera infectiosa*, or the earliest cases of an epidemic, might easily be confounded with these affections. Some of these diseases and conditions are sufficiently like cholera to receive the descriptive term "choleriform."

Manson states (p. 365, Tropical Diseases) that "it may be laid down that epidemic diarrhea attended with a case mortality of over fifty percent. is cholera." This seems to me to be an accurate statement and I can conceive of no epidemic diarrheal disease

in which the mortality approaches this figure, except an occasional and particularly virulent outbreak of epidemic dysentery of the specific infectious variety. (See Dysentery.) The nonepidemic diseases and conditions most closely simulating cholera and liable to be mistaken for it, are cholera nostras, ptomain poisoning, mushroom poisoning, choleriform malarial attacks, and acute metallic poisoning by arsenic, antimony and mercury. The first named disease, cholera nostras, more popularly known as cholera morbus, may occasionally be clinically indistinguishable from true cholera and may even terminate fatally in a few hours, but as a rule it is a far less serious affection and the prognosis is favorable. This disease was formerly believed to be caused by the vibrio proteus but this view has been abandoned.

Poisoning by mushrooms and ptomains and acute metallic poisoning are usually to be differentiated by the history and by the appearance of the stools and vomitus, which may contain particles of mushrooms or of the article of diet giving rise to the ptomain poisoning. In the case of acute metallic poisoning, blood may also be present in the vomitus or stools, and the chemical tests for the metals may throw light upon the diagnosis. In none of these conditions is the cholera spirillum to be found, while it is readily demonstrated in specimens direct from the stools and vomitus in most cases of cholera and invariably after culture. In pernicious choleriform malarial attacks the hemameba malariæ is demonstrable in the blood (not always in the peripheral current however) and melanemia, pigment either free in the plasma or included in leucocytes, will be present. There is, of course, no reason why the subject of malarial disease may not be infected with cholera, in which case malarial organisms will appear in the blood and cholera spirilla in the stools.

The blood serum of cholera patients, after the second day, will agglutinate cultures of cholera spirilla even in dilutions of 1 : 120. The reaction is obtained in the same manner as is the Widal reaction in typhoid fever. It is reliable but unfortunately appears too late to be of great diagnostic value.

Symptoms and Treatment. The symptoms of cholera may

vary considerably in degree of intensity, in individual cases. In all epidemics of cholera infectiosa there occur mild cases of the disease which depart from the classic program. In some of these cases one or more of the cardinal symptoms are absent and the observer may be deceived, by the apparent mildness of the attack, into the belief that the disease is not cholera. The only safe rule is to isolate and treat all cases in which cholera spirilla occur in the stools, as if the symptoms were grave. As a matter of fact, a mild case may give rise to a fulminant one in the next individual attacked. These atypical cases are often referred to as "cholerine" and for some undetermined reason they are apt to occur in the earliest days of an epidemic. They bear a relation to cholera similar to that which atypical or abortive cases of typhoid fever bear to enteric fever as it is usually observed.

The disease may be divided into three stages: Invasion, collapse and reaction.

There is no clear line of demarcation between the first two stages. The period of incubation varies from a very few hours to five days, although a few cases have occurred as late as ten days after infection. From twenty-four to forty-eight hours is the usual duration of the invasion or incubation period. Anorexia, headache, colicky pains and diarrhea usually mark the onset, the temperature remaining normal during the early hours. Violent purging and vomiting next ensue, with severe cramps of the muscles, especially those of the calves, fingers and toes. The early vomiting is projectile and the fluid vomited and dejected may be enormous in amount and soon clears the stomach and intestines of all traces of food or fecal matter, the stools taking on the characteristic rice-water appearance described above.

The body tissues are completely drained and the skin becomes wrinkled. As collapse ensues the radial pulse becomes almost indistinguishable, the features become pinched and livid, the surface temperature, as indicated by the thermometer, drops rapidly, sometimes reaching 92° F., the breath being icy-cold. At the same time the thermometer in the rectum will indicate an elevation of from 2° to 5° F. above the normal. In a few rare cases the rectal temperature

rises to 109° F., the axillary thermometer indicating 107° F. These cases are, of course, promptly fatal.

Prostration is profound. The voice becomes husky and finally aphonia occurs. The kidneys cease to perform their function; the urine may show albumin early and complete anuria may occur so that it is impossible to secure a specimen of urine by catheter. The mentality is usually preserved until death is at hand and the patient is restless and complains of great thirst and oppression in the chest.

The evacuations are painless at first but later tenesmus occurs. In a certain class of fulminant cases the toxemia occurs so early, and is so overwhelming, that the patient dies almost without a bowel movement. These are the cases of *cholera sicca*, or dry cholera, so called. In dry cholera the intestine is found, postmortem, to be full of the characteristic fluid. Collapse lasts for a few hours only and may end in coma and death, or in reaction, which is evidenced by increasing pulse volume, abatement of vomiting, a decrease in the number and an increase in the solidity of the bowel movements, the return of color, the disappearance of cramps, the reestablishing of the kidney function, restoration of body warmth and rapid convalescence. Or it may be followed by a partial restoration of the normal vital functions, the typhoid state and eventually death from uremia. This "cholera-typhoid" may last from a few days to two weeks, the symptoms being fever, delirium and diarrhea and it may terminate in death or in a slow recovery. Such cases may develop the usual complications and sequelæ of typhoid fever.

The discussion of the *curative treatment* of cholera could be spread over many pages. The very extent of the literature upon the subject emphasizes the fact that none of the thousand and one drugs and agencies suggested, has proved itself to be ideal, or reliable, or even more than doubtfully useful. Speaking of treatment in his recent book upon "Climate and Health in Warm Countries" (p. 141) Lieutenant-Colonel Giles of the Indian Medical Service says: "It must be in the first place remembered that it is absolutely useless to worry the patient with attempts to

administer medicines by the mouth, as the digestive and absorptive functions are for the time totally stopped, and it is quite as much to the purpose to put your remedies into the patient's pocket as to force him to swallow them. To have any chance of acting medicines must be administered by being injected beneath the skin by means of the hypodermic needle."

This teaching is sound, and coming from one whose observations of cholera, in its home (India), cover a quarter of a century, should be respectfully received and heeded. Manson (p. 373, Tropical Diseases) says: "Practically the only treatment of any proved value in cholera is the purely symptomatic and expectant one." Shakespeare (p. 893, Cholera in Europe and India) stated more than 15 years ago that: "Unless the so-called methods of hypodermoclysis and enteroclysis shall prove as effective as the recent experience of some Italian observers would seem to indicate, there appears to have been no marked advance made in the therapeutics of severe attacks of cholera." Upon page 899 of the same work, this scholar, now deceased, uttered a prophecy which bids fair to be realized, in the following words: "It has been shown that the chemical products of virulent cultures of the bacilli of cholera, as well as the chemical products of certain other specific pathogenic bacteria, possess the etiological and prophylactic powers of the living bacteria. In view of the progress of recent discovery in this direction, it does not seem at all improbable that in the near future the chemical poison of cholera, elaborated during the artificial growth and development of the comma bacillus of Koch, and extracted in a pure form, may become our most potent and ready weapon of defense against the devastations of cholera infectiosa."

In 1903, Strong, in American Medicine, August 15, wrote that: "The outlook is encouraging for the production of a safe method for immunizing healthy persons from cholera during an epidemic."

In the foregoing quotation Shakespeare did not predict the use of an antitoxic serum derived from immunized animals, but his statements concerning the prophylactic use of toxins may be said almost to have come to pass already, while, with the exception of the serum curative treatment, the efficiency of which cannot

yet be accepted as completely proved, it is still true that "there appears to have been no marked advance in the therapeutics of severe attacks of cholera."

Did therapeutic advance mean the suggestion of new drugs, then indeed might we claim to occupy an advanced position in the drug treatment of cholera. But the melancholy fact is that the mortality of the disease when treated by drugs remains today about the same as it was twenty-five years ago. In the light of this fact there can be no benefit in discussing these drugs from a curative viewpoint. I do not, however, advocate the abandonment of drugs in the treatment of cholera, but their use with the view of *curing* the disease does not offer us much encouragement in the present state of our knowledge. They should be used to combat symptoms and, except in the very mildest varieties of the disease or the premonitory diarrhea which sometimes precedes the grave symptoms, they should never be given by mouth.

The other routes available are by the rectum, in enemata, and through the skin, by needle.

Bearing in mind that the toxins produce collapse by circulation in the blood, we must seek to carry our remedies to that fluid. The usual route via. the mouth, stomach, intestine and absorbents is unavailable, the current being reversed by reason of the toxemia. All the tissues are emptying themselves into the intestine and we can expect no absorption of drugs into the blood from that viscus. The same is true to a certain degree of the tissues surrounding the blood vessels, although it is possible to make decided impressions by the hypodermatic route as evidenced by the hypodermatic use of the antitoxin, such alkaloids as atropine and morphine, and by hypodermoclysis. The route of injection directly into the venous or lymphatic systems offers the best promise in any case.

The introduction of antiseptic solutions within the small intestine, to destroy the spirilla of cholera, is rational from a theoretic point of view, but practically unattainable on account of the barriers offered by the ileocecal valve on one side and an intolerant stomach on the other. All efforts at antiseptic medication in cholera have been disappointing.

It is interesting to know that so long ago as 1832, when cholera appeared in Paris, M. P. Ch. A. Louis and his contemporaries made use of saline injections (in reality saline colonic flushings) in the collapse stage of cholera. In a valued book in my possession, published in 1835, as a memorial to his son, by Jas. Jackson, M. D., Professor of the Theory and Practice of Physic in Harvard College, there appears a series of letters written from Europe by Jas. Jackson, Jr., M. D., descriptive of the epidemic which devastated Paris in 1832. The clinical and pathological appearances of cholera are there described in a style and manner which would do credit to a medical writer of the present day. The use of saline injections is frequently mentioned and a case is cited in which fifty-one pounds of a saline solution was injected and followed by recovery. It will thus be apparent that this lately revived practice is nearly as old as our knowledge of cholera.

We may, however, combat collapse and the algid state by the use of external heat; profuse evacuations by astringent enemata; failing circulation by alcohol, nitroglycerine and alkaloidal stimulants by needle and by intravenous injections of normal saline solution; failing kidney function by the hot pack or sinapisms over the loins; cramps by small hypodermatic injections of morphine, or by brief inhalations of chloroform, or by five grain doses of chloral dissolved in water and injected under the skin every few minutes until half a dram has been so given. Of the drugs sometimes administered by mouth, Squibb's cholera mixture and chlorodyne are useful for cramps and cocaine, in doses up to one-third of a grain, may be helpful to control vomiting.

To recapitulate: Treatment is divided into prophylactic treatment and treatment of the attack. Prophylaxis has already been considered under the subtitle of etiology but a brief summary may be given here. A limited immunity from subsequent infection is conferred by an attack of cholera. Immunizing inoculations of cholera toxin, according to the Japanese method described above, probably confer the highest degree of individual immunity. Isolation of cases is imperative. All contaminated clothing

and all bed linen must be burned or boiled. All drinking water must be boiled. The hands and persons of attendants, doctors and nurses, must be disinfected by scrubbing with soap and water and by immersion and scrubbing in a solution of bichloride of mercury 1:2000. The use of uncooked food is dangerous, in time of epidemic, owing to the frequent conveyance of the cholera spirilla thereby. The disinfection or incineration of all dejecta and vomitus from cholera cases is imperative. Treatment with a five percent. solution of carbolic acid for half an hour, followed by burial, affords adequate disinfection of stools but incineration in a crematory is better when possible.

The treatment of the attack divides itself into the treatment of the three stages: Invasion, collapse, and reaction. Probably the most valuable treatment is the antitoxic serum treatment of the Japanese described above. It should be administered in the invasion stage, when possible, but should not be withheld later. The drug treatment has been given. Additional drugs of value, when oral administration is possible, are aromatic spirits of ammonia in dram doses, well diluted, for depressed circulation, and citric acid early, in the form of lemonade, to destroy cholera spirilla in the stomach and to render acid the intestinal contents, to inhibit the growth of spirilla there. High enemata of two quarts of warm water containing a half dram each of laudanum and tannic acid may be used advantageously. The body temperature may be kept up by immersion in the warm bath which should be maintained at 100° F., or by hot water in bottles, or by heated bricks. To administer hypodermoclysis of saline solution use a trocar needle attached to the rubber tube of a fountain syringe and slowly introduce the solution up to the amount of a quart and a half or two quarts, using both axillary and subclavicular regions. Repeat in a few hours if desirable. The solution may be extemporized by dissolving forty grains of salt (sodium chloride) in a pint of warm sterile water. During injection the temperature of the solution should be maintained at normal body heat or a little higher. If intravenous injections be made, observe great care in the matters of temperature, rate of flow, pressure and asepsis.

In the stage of reaction the treatment should consist of diets, intestinal irrigations with antiseptic solutions, intestinal antiseptic drugs by mouth, digestants and anti-anemic remedies. If cholera-typhoid occurs the treatment must be highly supportant as well.

LABORATORY DETECTION AND IDENTIFICATION OF THE CHOLERA ORGANISM.

Cholera spirillum. (*Koch.*) *Comma bacillus.*

Found.	In intestines and stomachs of individuals with cholera.
Morphology.	Short comma-curved rods one or two microns long and one-third of a micron in breadth, with polar flagella. In smears from the intestine they occur in parallel arrangement; in culture in variable arrangement.
Motility.	Actively motile.
Growth.	Rapid on gelatine plates and slant tubes, in alkaline peptone bouillon and on potato.
Aerobiosis.	Grows in presence or absence of oxygen but best in its presence.
Stains.	With basic aniline dyes, methyl blue and fuchsin.
Reproduction.	By fission.
Pathogenesis.	Causes cholera in man. Will cause the disease experimentally in guinea pigs.

For the prompt and practical identification of the cholera organism its reproduction in animals is not essential. According to Shakespeare, however (p. 676, Cholera in Europe and India), "For distinction between the curved bacilli of cholera infectiosa and other curved bacilli it is a sine qua non that plate cultures, tube cultures and potato cultures be resorted to in addition to microscopic examination." The cholera-red reaction, which is always present in pure cultures, should be elicited also as a confirmatory test. The essential procedures, then, include recovery of the organisms from intestinal or stomach contents, cultivation upon gelatine plates and slant tubes in alkaline peptone bouillon and upon steamed potato. Proceed as follows: Sterilize a platinum

wire loop in an alcohol or Bunsen flame, cool an instant and transfer a loopful of liquid contents of the intestine, or of vomitus, or one of the whitish flakes from the intestinal contents, to a clean slide; permit evaporation for a few moments and then drop upon the specimen a clean cover-glass upon which has been placed a minute drop of a very dilute fuchsin or methyl blue stain. Examine at once with an oil immersion lens ($\frac{1}{12}$).

The bacteria, still alive, should be stained and show the parallel arrangement referred to above if in pure culture, as is sometimes the case. The cholera spirilla will probably be outnumbered by various other bacteria, however, and there may not be more than two or three spirilla to a field. The staining will not of course be limited to the cholera spirilla. The staining process in this connection may be omitted if desired. The spirilla should be motile and should appear as in Fig. 14.

Next proceed to inoculate with a flame-sterilized platinum loop, dipped into the fluid contents of the intestine (ileum by preference), the surface of sterile gelatine plates and cylinders of sterilized steamed potatoes in test-tubes. The slant gelatine tubes should be inoculated by a puncture incision with a platinum wire or needle. The alkaline peptone bouillon should be inoculated with a flake from the suspected material or a loopful of the same.

In tropic countries incubation is not absolutely essential but where marked diurnal variations of temperature occur the incubator should be used and a temperature of 37° C. should be maintained. At the end of twelve hours cloudiness of the liquid culture will be observed and a thin pellicle will appear at the surface. Upon the gelatine surfaces white points will appear in less than twenty-four hours and the growth on potato will be of a grayish or slightly brownish color with an appearance like porcelain. Old gelatine plate colonies take on a roseate hue (p. 353, Tropical Disease, Manson), said to be characteristic. The stab culture will present the appearance described in the text and pictured under etiology. All should yield curved rods at this time. Shakespeare considers the potato growth of curved bacilli as positively diagnostic (p. 675, Cholera in Europe and India). If pure cultures

are not obtained at the first effort careful reinoculation of media should be made from the points of growth. The illustrations indicate the naked eye appearance of these growths, and the microscopic appearance of a pure culture of cholera spirilla.

At the end of twenty-four hours the cholera-red test may be made from the peptone bouillon culture in the following manner: To a tube of the culture add a few drops of pure sulphuric acid (C.P.). A color reaction varying from pink to red appears, due to the action of the acid upon the indol and nitrite present in the culture. Failure to secure the cholera-red reaction may be due to faulty peptone and this element of error should be guarded against by testing the peptone bouillon before hand with a known pure culture of cholera spirilla. If failure with this pure culture occurs the peptone should be rejected.

Formulæ and directions for the preparation of media, gelatine plates and slant tubes, peptone bouillon and potato will be found in the Appendix. In pure culture, true spirals, as well as U and S formations, may occur from end-to-end arrangement. Involution forms appear in old cultures. They are very variable in shape and stain indifferently. Strict surgical cleanliness—asepsis—must be observed in the handling of specimens and cultures of cholera spirilla to avoid self-infection. This accident has occurred in the laboratory more than once and the possibility of it is a real danger. The fact that cases of cholera have so originated should, however, convince the most skeptical that the disease is due to the organism of Koch.

CHAPTER II.

BERIBERI.

Synonym. Kakké.

Definition. In taking up the disease, beriberi, I propose to depart from the usual definition found in text-books and reference books. There have been carried out during the last five years certain important studies as to the nature and causation of beriberi which justify us in looking upon this disease as something more than the peripheral multiple neuritis usually described, which condition is, in all probability, a sequel or a late stage of beriberi. This notable discovery, for so it deserves to be called, is largely the result of one man's work. Dr. Hamilton Wright, Late Director of the Institute for Medical Research, Federated Malay States, has worked out the clinic and pathologic facts in many carefully studied cases and has fitted a causation theory to them, reversing the usual rule of attempting to fit facts to a theory. The result is a convincing array of matter that bears the hall-mark of truth.

Manson points to the fact that long ago Norman Chevers announced a theory of beriberi causation similar to that now proposed by Wright. The credit must nevertheless be accorded to Wright, a graduate of McGill University, Montreal, and an honorary fellow of Johns Hopkins University, for his very thorough, painstaking, and withal, conservative work of analysis and construction.

I shall follow his classification and ideas in this article so far as I can accept them as proven.

Beriberi is an acute or subacute infectious disease of the tropics and subtropics, occurring in epidemics and endemically. It is characterized by a primary gastro-duodenitis of varying intensity and by a secondary toxic degeneration of the nervous elements

of parts of both central and peripheral nervous systems, manifesting itself by neuritis and palsies of various degrees and locations, according to the particular nerve tracts involved. It is probably contagious. The most apparent symptoms, except in acute fulminating cases, are those of the secondary involvement of the nervous system, and include neuritis, paralysis, muscular atrophy, dropsical effusion and cardiac disturbances, both as to rhythm and valvular competence. In the acute fulminating cases, symptoms referable to the primary gastro-duodenitis are well marked and include an oppressive sensation in the stomach with nausea, epigastric pain on pressure, some bulging of the epigastrium, slight fever and some congestion of the pharynx. The disease is attended with a variable mortality of from five to thirty percent. and results in death, recovery with permanent neuritis or paralysis, or in complete recovery with regeneration of the involved nervous tracts and restoration of function. It attacks persons of all races, sexes, and ages, but it is distinctly a place infection and most common in communities of confined people, living amid crowded and unsanitary conditions, as, for example, in prisons, ships, barracks and asylums. It does not, however, particularly select the sick, aged or decrepit for its victims, being commonest between the ages of twenty and forty years.

Facts of Geography and History. The geography of the distribution of beriberi is the geography of the tropics and subtropics, viz., that portion of the earth's surface lying between the thirty-fifth parallels, north and south of the equator. In addition to this it is frequently carried by sea to temperate ports and countries.

It has been recognized in all of the countries comprising the American tropics, Cuba, Porto Rico, Central America, the Panama Canal Zone, and the Hawaiian and Philippine Islands. It is also frequently encountered in many North American ports and the continents of Europe, Africa, Asia and South America all furnish original cases. The islands of Japan and Australia also present the disease in epidemics and endemics. Occasionally an institutional epidemic outbreak occurs in a temperate country, but rarely, if ever, in this country. It will not be surprising, however,

if endemic instances of beriberi are found in the United States, as beriberic symptoms may easily be confounded with those of various spinal cord diseases, which are common enough in the United States, as one may easily convince himself by visiting the outpatient clinics of our large city hospitals.

The Malay Peninsula is a veritable hot-bed for beriberi and it was here that the work of Hamilton Wright, already referred to, was carried out. This region is a hot-bed in another sense also, being a low-lying, moist country under a tropic sun, and it presents ideal conditions for the incubation and propagation of germ life generally. The same statements are true concerning certain parts of the Philippine archipelago and here, also, beriberi is a common disease.

The principal historical fact of interest concerning the disease is that it was early recognized by the Dutch colonists in the East Indies, and later by the British in India, as a peculiar disease. Within the past fifty years much clinic and pathologic data has been accumulated by observers in tropic regions all over the world and notably in Japan, also. The theories of causation which have been announced from time to time have covered a wide range, and although some of them are still proposed in explanation of the beriberic phenomena they may be considered as interesting chiefly from an historic standpoint and properly, therefore, may be mentioned here. Only the most plausible theories advanced will be stated. Most of them have gone down before the tests of experimentation. The list of supposed causes includes arsenic poisoning; a fish diet (infected, raw or decayed fish); poisoning from a principle developed in growing rice (as ergot develops in growing rye and gives rise to ergotism); blood parasites; bacteria in the blood; fat starvation; nitrogen starvation; anemia; intestinal parasites; and the toxic exhalations of a saprophytic germ.

In pamphlet No. 1, Vol. II, of "Studies from the Institute for Medical Research, Federated Malay States," there will be found (pp. 60–61–62) the details of Wright's experiments to determine the truth or fallacy of ten of the most prominently advanced theories of causation of beriberi. In this list are included most of

the above mentioned theories and the conclusions reached are based upon experiments, conducted without prejudice, and establish the fallacies of each proposition. The experiments need not be detailed here but it may be interesting for the student to refer to them.

Troops stationed in the tropics are apt to suffer from this disease, particularly those in the East Indies, Japan, and China, but white troops, doubtless because of their more hygienic environment, manner of life, and less crowded quarters, suffer far less than Malays and Mongolians. In our army in the Philippines white men seldom acquire beriberi, but it has been common enough in native troops and especially among native prisoners. According to the published reports of the Surgeon-General, United States Army, for the year ending June 30, 1900, beriberi prevailed extensively among the Filipino prisoners of war at Cavite. In the same report is mentioned the first occurrence of the disease in a white American soldier. It terminated fatally in three months. Another case was reported the same year with the notation of having been returned to his quarters improved, after a month's treatment in the hospital.

Whether or not this patient was the one I subsequently saw in the United States General Hospital at San Francisco in January, 1901, I cannot say, but my first experience with beriberi was in a medical ward in that hospital, prior to my sailing for the Philippine Islands. There I had one case under my observation and care for about three months. The patient was a white American soldier who contracted the infection a year or more before in the Philippines, an abjectly helpless cripple with paralyzed and wasted limbs, absolutely devoid of sensation in some members, and exquisitely sensitive to touch, jar, movement, or temperature variations, in others. His heart was extremely erratic as to rhythm and there were two distinct murmurs present. He was given considerable morphine hypodermatically for the relief of the pains due to neuritis and was propped in an invalid's chair and wheeled into the open air daily. His mental state was excellent and his realization of his hopeless condition rendered his plight

more than usually pitiable. This case made a profound impression upon me and I always recall this man as the most complete beriberic wreck I have ever seen.

During the year ending June 30, 1901, one case was reported among the negro troops but none among the white soldiers. According to the same authority, however, about fifty percent. of all sickness among the Filipino prisoners of war during this year was due to beriberi.

Dr. F. L. R. Tetamore reported an epidemic among the native prisoners at Lingayen, Pangasinan Province, of 186 cases, of which 31 died, 20 were returned to duty, 45 were reported as convalescent and 90 remaining as sick. Seven postmortems revealed no constant lesions and cultural experiments developed no constant micro-organisms, although a diplococcus was obtained from the blood of the living and from cadavers. The necropsy notes do not mention the condition of stomach and duodenum.

During the following year no cases were reported among the troops, either white or colored, but an interesting report of one epidemic among native prisoners was presented by Lieutenant Waterhouse, United States Army, the medical officer at Malagi Island, Laguna de Bay, Luzon.

This island was set aside for prison purposes and was occupied on January 20, 1902, by a company of white troops, in charge of 100 native prisoners. There were no buildings nor evidences of former habitation at this time. The island contains 120 acres, is well drained and its highest point is 100 feet above the lake. Forty days after occupation two cases of beriberi arrived in a detachment of new prisoners. They were isolated at once, but efficient isolation was impossible. Lieutenant Waterhouse's report pointed to the contagious character of the disease and the reporter expressed a conviction that the disease is of bacterial origin. After the introduction of the two original cases new ones occurred at brief intervals until twenty-four cases, in all stages of the disease, were in this isolated camp. These cases were removed from the island, but fifty-nine more beriberic prisoners were discovered and liberated. Somewhat later forty more

cases were discovered. Six months after the occupation of the island all persons were liberated. All of the cases mentioned occurred during a period of about nine weeks. To quote Lieutenant Waterhouse (p. 100, Report of the Surgeon-General, United States Army, for 1902): "The theory of germ propagation and of infection by personal contact and by place infection appears to me to account more satisfactorily for the spread of the disease. To begin with we had 100 prisoners hard at work here for a month and a half without the slightest symptom of the disease; then two cases of beriberi were introduced, and after that the spread was steady." He points out that most of the cases came from one set of quarters, the first set erected, and that the barracks were high, airy, free from mosquitos and flies, and that a stiff breeze was usually present; also that the epidemic took place in the dry season. He concludes: "From the fact that none of the prisoners had developed beriberi prior to its introduction here from a known infected point, of the apparent spread by contact, and of the slight influence which diet appeared to exert over it, the presumption is that we are dealing with a disease of microbic origin, prone to attack those in a run-down and mentally depressed condition, and one which is conveyed by fomites and by close personal contact."

During the year ending June 30, 1904, there were reported from the United States Army, 636 cases of beriberi, distributed as follows: twenty-two white men, no negroes and 614 Filipinos. One admission occurred in the United States while all the others were reported from the Pacific Islands and China. The rate of admission in the Pacific Islands and China was 26.66 per thousand and the death rate was 1.05 per thousand men. The actual number of deaths was twenty-five, of whom three were white men and twenty-two were Filipinos. In addition to this there were disability discharges of both white men and Filipinos. Thus it will be seen that beriberi has become a morbific factor to be accounted with. When the Panama canal is well under way the disease is bound to cut some figure in the health reports from the canal zone. The disease is common in the city of Panama and causes many deaths.

In 1904, at the Louisiana Purchase Exposition at St. Louis, Mo., there occurred an interesting epidemic of beriberi among the 1276 Filipinos who were brought to the United States in connection with the Filipino exhibit and as members of the representative military organizations from the Philippine Islands. This epidemic is said to be the only one of record which has broken out in the United States and it is so reported in the Surgeon-General's report for the army for the year 1905. Captain L. P. Williamson, Assistant Surgeon, United States Army, reported fifty-nine cases with four deaths, as occurring among the entire strength. The Filipino Scouts, a military organization of 450 men, escaped infection completely, being quartered in a model camp which was conducted in strictest accordance with sanitary laws. The native Filipino civilians, to the number of 788, were at first subjected to conditions of extreme overcrowding and filth, in a single building, and the disease appeared under these circumstances. After the correction of these conditions beriberi disappeared, except that the constabulary organization, which remained in the building in which the epidemic first occurred, continued to furnish cases during its entire stay, a most suggestive fact pointing to the infection of the building, particularly as the natives who removed to their respective villages ceased to incur the disease.

Etiology. It has already been pointed out that sex and age are not determining causes in beriberi and that a tropic climate is not an absolutely essential condition for the disease. Occupation has no particular bearing in this matter, except when associated with overcrowding, which state favors intimate contact and infection. It cannot be said that the ultimate cause of beriberi is definitely known, but it is highly probable that it is a microbic organism which gains entrance to the body through ingested food or drink, through inspired air or through a lesion of the skin. The usual gateway of infection is, probably, the alimentary tract; the disease organism entering by way of the mouth, multiplies in the stomach and duodenum and elaborates a toxin which causes a local irritation or inflammation of the mucosa at the site of multiplication, usually the duodenum. The toxin is promptly ab-

sorbed and "poisons certain afferent and efferent neurones to different extents and different degrees."

Hamilton Wright calls attention to the similarity of the mode of action of the causal organisms of beriberi and diphtheria and points to the fact that the primary lesions in both diseases are necroses of epithelium, caused by powerful toxins elaborated at or near the sites of inflammation, and that these absorbed toxins have degenerative actions upon the peripheral endings of nerves, especially the cardiac terminations of the fibres of the pneumogastrics. He ventures the prediction that when isolated the beriberi organism will resemble the diphtheria bacillus.

As indicating a Japanese view of the causation of beriberi I quote the following from The Lancet of June 2, 1906, being a portion of the third lecture delivered by Baron Takaki, Late Director-General of the Medical Department of the Imperial Japanese Navy, at St. Thomas' Hospital, London, May 11, 1906, upon "The Preservation of Health Amongst the Personnel of the Japanese Navy and Army." Baron Takaki says:

"The health of our own army has been gradually improving in late years, but beriberi is not yet eradicated as it is in the navy, and I regret to state that although the cases are few in times of peace at home, the disease is apt to break out in time of war just at the time when stronger men are needed. In former years beriberi prevailed largely in the army, as it did in the navy, but now it occurs less frequently than before."

He submits a table showing the number of cases of beriberi per thousand men for a number of years. In 1903 the rate of occurrence was 14.63 per thousand. Takaki considers the great diminution in the number of cases of beriberi in 1885, in a certain division of the army, to be the result of the adoption of a ration of rice with barley, in the proportion of seven to three. (In 1883 the rate of occurrence was 144.82 cases per thousand men and in 1885 it had dropped to 3.08 cases per thousand men.) This led to the experimental use of barley with rice in other divisions and the rate for the year 1903 (14.63 per thousand) is believed by Takaki to be the result. The rate per thousand is not given for

the Russo-Japanese war period but the total number of new cases for this period, 97,572, indicates something of the havoc wrought by the disease and the high rate per thousand of Japanese soldiers engaged. Continuing, the Baron says:

"Unfortunately, during the Chinese-Japanese war and the beginning of the Russo-Japanese war, owing to circumstances, only rice was given to the men as principal food, and as a consequence cases of beriberi increased greatly—in fact there was a very much larger number of cases than usual. But in the later period of the Russo-Japanese war when we began to give the men barley with rice, and increased the quantity of meat, the cases of beriberi decreased rapidly with the change of diet. Another illustration of the influence of diet upon the health of the men is shown by the fact that there was no case of berberi among the soldiers of the naval brigade during the siege of Port Arthur, although there was a large number of cases of beriberi in the army. These men lived among the soldiers and under exactly the same conditions, but they differed from the soldiers in one respect, that they were supplied with 1 pound of meat, 10 ounces of barley, and 20 ounces of rice per day, while the soldiers were supplied with 5 ounces of meat, and 30 ounces of rice per day. The above example confirms my view that beriberi largely occurs among men who are fed with an insufficient quantity of nitrogenous food and an excess of carbohydrates."

Table XVII, submitted by Takaki, shows the number of infectious cases and of beriberi patients from the beginning of the war in 1904 to the last day of August, 1905.

Disease.	New Cases.	Deaths.
Smallpox	347	33
Scarlet fever	10	2
Typhus fever	51	11
Diphtheria	9	1
Typhoid fever	9722	4073
Dysentery	7642	1804
Beriberi	97,572	3956

In this interesting tabulation typhoid fever maintains its old-time reputation as the "Destroyer of Armies," having caused a greater number of deaths than any other disease, but beriberi establishes a new record as a disabling military disease, the number of cases reported being almost exactly ten times the number of reported typhoid cases.

Pathology. According to Wright's views, the great majority of beriberi cases come to necropsy in the stage or condition of paralysis or neuritis, in reality a postberiberic state. The mass of statistics concerning the disease has been gathered from post-beriberic studies. He points out that it would be as reasonable to build up the pathology of diphtheria from the postmortem appearances of postdiphtheritic paralysis as to build up the pathology of beriberi from postberiberic changes.

Under the subsection upon symptoms we will take up Wright's classification of the disease into (a) acute pernicious beriberi, (b) acute beriberi, (c) subacute beriberi, and (d) beriberic residual paralysis or neuritis, and the pathological changes will be given here according to this classification.

In *acute pernicious beriberi* the pharynx is generally reddened and the abdomen, thorax and pericardium contain varying amounts of clear, staw-colored fluid. The mucosa of the pyloric end of the stomach and of the duodenum (and rarely a portion of the jejunum and ileum) is congested, highly inflamed or even eroded, the summits of the transverse rugæ of the duodenum and the pylorus showing discrete or confluent hemorrhagic extravasation or simply deep injection. The naked eye appearances are those of acute inflammation (a gastro-duodenitis), and the microscopic appearances indicate the same condition, showing small-celled infiltration, cloudy degeneration and necrosis of the mucosal epithelium. Polymorphonuclear leucocytes are always present and swelling of adjacent mesenteric glands is common but not constant. These glands do not contain bacteria. Lungs, liver, kidneys and spleen show varying degrees of congestion but no characteristic changes. The heart is dilated and flabby, collapsing when cleared of blood clots, and microscopically shows

fatty changes, most advanced in cases of a week's standing or longer, and there is more or less dissociation of the muscle fibres. There is abundant microscopic evidence that almost the entire cardiac nervous system is affected with beginning atrophy, the effect of the beriberi toxin.

Petechiæ of the heart's surfaces are common, and incompetent tricuspid valves are often found. The edema will probably be slight and localized, unless the disease has persisted for a week or two, but at times a general dropsy may develop quickly. Whether the transudation of serum through the vessel walls into the surrounding tissues is solely due to the paralyzing effect of the toxin upon the nervi-vasorum, is as yet an undecided point. Organic changes of beginning atrophy are present at any rate.

There are no distinctive blood changes. Leucocytosis is common but not constant, and anemia is not usually marked.

Patients seldom die during *acute beriberi* and consequently the opportunities for pathologic studies are rare. Doubtless the gastro-duodenal changes would be found to be similar in kind but less intense in degree, if postmortems were possible in the acute stage.

If death occurred in the (c) *subacute stage of beriberi* the gastro-duodenal lesions would probably not be apparent. Except in the acute pernicious variety deaths practically occur only in the postberiberic stage or the state of (d) *beriberic residual paralysis or neuritis.* To quote from Wright (p. 8, No. 2, Vol. 2, Studies from Institute for Medical Research, Federated Malay States): "As a matter of fact the beriberic residual paralytic is simply a nervous wreck whose active cause has long since accomplished its work and departed. A gastro-duodenitis is never seen. Mesenteric glands are never found swollen; petechiæ are not to be observed in the serous membranes. . . . In fact there are no positive signs of an acute process in any organ of the body."

The changes in the nervous system are extensive and important. There is advanced atrophy of the peripheral nerve fibres extending upward towards the cord and a degeneration (secondary?) of certain cells of the cord, from which the atrophied nerve fibres

originate. The posterior nerve roots as well as certain of the columns and the cells of the anterior horns of the cord may also show atrophy.

In edematous cases the nervi-vasorum of vessels in the areas of edema show advanced atrophy. Muscular atrophy and degeneration (fatty) are present in all muscles supplied by the affected nerves. These changes in the nerves and muscles are those observed in any multiple toxic neuritis, alcoholic, metallic, diphtheritic, etc., and are usually bilateral and symmetric.

The degree of regeneration in nerve tracts which has taken place in any given case, will also determine the pathologic condition found. The heart in beriberic residual paralysis will be flabby, it may show fatty degeneration, and in the event of previous valvular incompetence there may be a compensatory hypertrophy. The lungs may be edematous and the pericardium and abdomen may contain serous effusions.

Symptoms. Before proceeding to the discussion of symptoms let us briefly consider some of the schemes of classification which have been proposed. They are numerous, but few of them are based upon scientific principles and most of them are incoherent and useless. Scheube, a careful student of beriberi with extensive opportunities for observation of the disease in Japan, has proposed a classification, which, while purely clinical, is useful in grouping cases. It overlooks, however, the cardinal distinctions between symptoms of the *disease, beriberi,* and manifestations of the effects of the beriberi toxin, pathologic conditions which are in reality *postberiberic symptoms.* These distinctions must be granted if we accept Wright's work and conclusions. Scheube's classification groups beriberic cases into:—

1. The incomplete, chronic relapsing, imperfect or rudimentary cases. (Including "mixed" beriberi.)
2. The atrophic form—dry beriberi.
3. The edematous form—wet beriberi.
4. The acute pernicious form—fulminating beriberi.

In view of the fact that all of these types (except the fulminating type) blend and overlap, and that the type of today may sud-

denly change to another tomorrow, it is plainly impossible to formulate any satisfactory classification based on symptoms.

Hamilton Wright's classification of beriberi into four varieties is based upon underlying pathologic conditions, and is as follows:—

1. Acute pernicious beriberi (fulminating).
2. Acute beriberi.
3. Subacute beriberi.
4. Beriberic residual paralysis or neuritis.

In **acute pernicious beriberi** the symptoms are those of gastro-duodenal irritation of greater or less intensity, and of cardiac paralysis. The onset is sudden and the fatal termination can usually be foreseen early. There may be accompanying respiratory, vaso-motor and sensory paralysis and the duration of the disease may be less than twenty-four hours and rarely extends beyond two weeks. This fatal and pernicious form of beriberi may suddenly develop in the course of a subacute case.

The **acute** variety is marked by a less sudden onset and less prominent gastro-duodenal signs and paretic symptoms. Heart involvement is usually present but the prognosis is neither so grave nor so apparent as in the pernicious variety.

Subacute beriberi is even more gradual in its onset. The paretic symptoms do not noticeably affect the heart and may be limited to slight loss of power and sensation and vaso-motor paralysis, commonly noticed in the regions supplied by the anterior tibial nerves. The gastro-duodenal symptoms may be entirely overlooked.

Beriberic residual paralysis or neuritis is the disease as it appears after all signs of gastro-duodenal irritation have disappeared and after (presumably) the disappearance of the specific organism and its toxin. The paralysis or neuritis is the accomplished work of the toxin.

Let us now consider specimen cases of each of these four types.

In **acute pernicious or fulminating beriberi** the patient, if observed from the onset of the disease, will present symptoms somewhat as follows: There first appear failing appetite, epigastric discomfort and slight nausea, often considered dyspeptic at first,

increasing within a few hours to pain upon pressure over the epigastrium and shortly followed by slight bulging in this region. Moderate congestion of the pharynx with anesthesia early develops. A degree or more of fever may be noticed if the temperature is taken early. Dyspnea, restlessness and sometimes

Fig. 17 —Mixed Beriberi. (From report of Surgeon-General, U. S. A., for 1901. By permission.)

progressive aphonia are present. Areas of anesthesia may be discovered early but the patient will not call attention to them nor be conscious of them. The pulse rate is at first increased. There may be cramps in the feet and legs, formication or sensa-

tions of numbness or pricking, foot drop, loss of ability to abduct or adduct the thighs, loss of tactile sensation and of the heat and cold sense. Alteration in the knee jerks, possibly exaggeration of one or both at first, is followed by rapidly developing complete loss of the reflex. The pulse rate is increased to 100 and upon exertion may reach 130. A systolic murmur appears at the apex

Fig. 18.—A. Mixed Beriberi. B. Wet Beriberi. C. Dry Beriberi. (From report of Surgeon-General of the Army, 1901. By permission.)

of the heart and the normal spacing of the sounds is lost, the abnormal spacing becoming even, like the ticking of a clock. Vomiting may occur and death may come suddenly from heart paralysis. It will usually be found that pretibial edema, at least, has developed even within two or three days, and almost from the first

the calves of the legs are painful to pressure. This chain of symptoms may develop almost within a day, Gerrard ("Essay on Beriberi") citing a case of his which lived but sixteen hours after the commencement of the attack.

The development of heart paralysis may be so sudden as to cause death before general paralytic symptoms appear. There is practically a race between the pneumogastrics and the other nerves of the body as to which shall first succumb to the beriberi toxin and the appearance, or nonappearance, of the above mentioned paretic symptoms depends upon the rapidity with which the toxin paralyses the vagi and causes death. General weakness and paralysis usually develop, however, before the pneumogastric and its dependent vital functions completely succumb.

Clinically **acute beriberi** is less rapid in its onset and progress, and less grave as to its immediate prognosis, although serious enough as to the ultimate results. There is usually a period marked by failing appetite and vague dyspeptic pains, corresponding with the period of irritation or inflammation of the stomach and duodenum, less decided than in the pernicious type but fairly well defined. The toxic involvement of the pneumogastric nerves is slower in occurrence and of a less intense degree, but concurrently there occurs a group of paralytic symptoms, invariably due to poisoned nerves and centers by the beriberi toxin, widely distributed through the body and accompanied by edema, often of considerable volume. These paralyses are often incomplete but sensation is much altered and anesthesia widespread, the cranial nerves of sensation often being poisoned. Paralyses of the throat and larynx are less common and the heart disturbance, while well enough marked, is not so profound, nor is the paralysis so complete, as in the pernicious type. Most acute cases survive this stage and die, if at all, in the postberberic stage (residual paralysis) or from intercurrent disease. The appetite usually returns and the dyspeptic symptoms pass away but the cardiac paralytic symptoms remain, the heart showing signs of dilatation.

The subject of **subacute beriberi** may suffer for a week or more

with dyspeptic symptoms and loss of appetite before any other signs of disease become manifest. There may be slight tenderness upon deep pressure in the epigastrium, but little else than the failing appetite and dyspeptic symptoms will usually be noticed and even these may escape attention. Disturbances of sensation may next appear, preceded, perhaps, by a slight and brief rise of temperature. Tender nerve trunks, especially in the legs, will next appear, and pretibial edema, with weakness, numbness and wasting of the muscles supplied by the involved nerves, will be progressive to the point of actual paralysis, or the process may stop before this stage is reached and the tenderness and loss of power may remain stationary, or gradually abate. The knee jerks disappear and foot drop is extremely common. The superficial reflexes may be exaggerated, diminished or absent but they usually respond to severe stimulation, while there is usually delay in the conduction of nerve impulses. The heart will probably be normal to all appearances, except for an increased rate of pulsation. The reaction of degeneration to electrical stimulation will be present in affected muscles early. Loss of co-ordinating power, with particular reference to station and to locomotion, is noted. The signs of indigestion appear early and the bowel function is usually well preserved. This variety of beriberi is prone to relapse or recur, indicating a reinfection or a relighting of an old infection. The progress of these cases is towards recovery, rapid or slow, the persistence of some degree of paralysis depending upon the rate and degree of regeneration of poisoned nerves. The "rudimentary" cases of Scheube may be classed with the subacute cases of Hamilton Wright.

In the military hospital at La Guane, Island of Samar, Philippine Islands, in July, 1902, I saw fifteen cases of beriberi, mostly of the type just described, through the courtesy of the surgeon, Captain Weirick, United States Volunteers.

All were native Filipino soldiers or prisoners. In Tacloban, Island of Leyte, Philippine Islands, in the same month I saw two cases of the very mildest type, thereto unrecognized, aboard a small sailing vessel in port. Both were Filipino sailors, sleeping

together in a small cabin aboard the boat. Neither one was entirely incapacitated for work.

The subject of the remaining variety, **residual beriberic paralysis or neuritis,** will present a more or less definite history of one of the varieties already described and a clinical picture varying from the mildest paretic or neuritic manifestations to general paralysis,

Fig. 19.—Wet Beriberi. (From the report of the Surgeon-General, U. S. A., for 1901. By permission.)

with local edema or general anasarca. As an example of this type let us select a moderately severe case. With a history of acute or subacute beriberi as described above, some time within the preceding year, the patient comes to us in the following condition: The special senses of sight, smell, hearing, and taste are not disturbed and sensation about the head is unimpaired. In the lower limbs it is practically absent and in the arms and hands

sensation is impaired and delayed. He moves his hands and arms freely, however, but there is marked loss of power in the legs and

Fig. 20.—Position taken in Mixed or Dry Beriberi. (From report of Surgeon-General, U. S. A., for 1901. By permission.)

feet, as regards extension and flexion; the gait is ataxic or spastic and station is uncertain. The respiratory muscles, diaphragm

and intercostals, perform their functions. Edema of the lower limbs extends to the scrotum and lower trunk and obscures the wasted condition of the affected leg muscles. The appetite and digestion are fair and there is no tenderness to pressure in the epigastrium. Pressure over the nerve trunks in the legs produces pain. The knee jerks are absent. The condition of the circulatory system is one of excitability, exertion increasing the pulse rate to 140 per minute, and the spacing of the heart sounds is even, as I have described it above. The veins of the neck appear to pulsate and the cardiac dulness is increased to the right. An apex systolic murmur is present and the aortic and pulmonary second sounds are reduplicated.

This man may remain in this condition without developing further edema, or he may even improve, or general anasarca may develop; or he may suddenly develop dyspnea and syncope and die.

It will be seen plainly that this picture may be varied almost indefinitely, according to the preponderance of the paralytic, neuritic or dropsical symptoms in any given case. It will serve however to illustrate the type of beriberic residual paralysis or neuritis.

We may now briefly review the symptoms of beriberi without special reference to the types of the disease just described. P. N. Gerrard, a co-worker with Hamilton Wright in the Malay Peninsula, and an observer of great experience, accepts the classification of Wright as an eminently satisfying one but in his "Essay on Beriberi" (London, 1904) expresses the opinion that, for students, the clinical classification according to Scheube and others is most useful. He describes cases as wet, mixed, dry, rudimentary, fulminating (acute pernicious) and spasmodic. After the dyspeptic symptoms and the brief accompanying fever, he notes weakness of the knees, numbness of the legs, and pretibial edema as developing within the first ten days and usually in the sequence named. The succeeding symptoms are not necessarily consecutive, nor do they always occur in the order named, and may be present either in whole or in part. Diarrhea,

pneumogastric crises (in pernicious cases), paralysis, vomiting and hiccoughs, bed sores and ulcerations, spasms or contractions, convulsions, laryngitis (subacute), tenderness upon pressure over nerve trunks (neuritis), dilatation of the heart, pericardial effusion, wasting of muscles, dyspnea, cyanosis, delirium cordis, edema of the lungs and syncope may occur.

Gerrard recognizes a certain variety of beriberi as spasmodic. This variety includes all cases in which incoordination appears, and choreiform spasms, absent during sleep, are described as occurring in affected parts upon attempts at movement. These cases are infrequent.

Muscular contractions naturally occur in paralytic cases of beriberi just as they occur in paralysis from other causes.

Prognosis. The prognosis of beriberi is most uncertain. Many cases recover; some completely, others incompletely. Sometimes the most discouraging cases make good recoveries, while at other times those apparently most promising die. The determining facts are the degree of involvement of nerves supplying vital organs, the amount of edema, the presence or absence of complicating infections and the environment of the patient. The fulminating cases nearly always die.

Diagnosis. The diagnosis of beriberi should be carefully made. Almost any toxic neuritis may simulate it, in at least some of its manifestations. Alcohol and arsenic produce some of its most conspicuous symptoms, as do lead and other metallic poisons. Malarial disease, nephritis and heart disease must be remembered, as producing some of its symptoms, as well as intestinal parasites. Nearly all of the common spinal cord diseases produce similar symptoms to those of beriberi and these diseases offer, perhaps, the greatest opportunities for diagnostic mistakes. Among them are nerve syphilis, lateral spinal sclerosis, ascending spinal paralysis (Landry's paralysis), myelitis and posterior spinal sclerosis (locomotor ataxia). The diagnosis of sporadic beriberi must always be a differential one. In the presence of an epidemic direct diagnosis may be possible. Points of value to be remembered are the absence of knee jerks, the tenderness of paralyzed parts

the muscular wasting, edema (especially pretibial), the impairment of sensation and the history and course of the disease.

Treatment. The treatment of beriberi should be considered under two heads: The prophylactic treatment and the medical treatment.

Under the first heading are included all measures looking to the prevention and control of epidemics. Whether we accept the doctrine of a microbic cause operating within the body or not, there is abundant evidence that the *materies morbi* clings to places and localities, and we have the choice of removing the inhabitants of these places to new and uncontaminated localities or of purifying and renovating the infected places by the most radical sanitary measures possible. Removal is the preferable plan and usually can be carried out, but exceptionally it is necessary to fight the disease without abandoning the infected place. In such cases all surfaces of buildings, floors, walls, ceilings, and the surface soil should be treated with strong germicidal solutions. Sanitary drainage and water-closets should be instituted, fresh paint and whitewash should be freely used, and all removable furniture, bedding and clothing, should be destroyed by fire. On general principles insects and vermin should be destroyed or excluded by mosquito netting, fumigation and other devices. Isolation of the sick from those in health, should be effected and cooked food (in the hot state) and sterilized water only, should be provided. If the place be abandoned, all furniture, bedding and clothing should be left behind and destroyed and new supplies issued. The closest watch for new cases should be kept up and the knee jerks and legs of all persons should be examined daily for signs of beriberi. Outdoor activity, reforms in feeding, ventilation, daily bathing, sunlight, freedom from crowding, and hygienic conditions generally, must be provided and insisted upon, under intelligent medical supervision. The forecastles and sleeping quarters aboard infected ships offer special difficulties to adequate disinfection.

Under medical treatment we include, beside drugs, all agents used to cure, palliate or relieve suffering. How much can be ac-

complished, either by drugs or mechanical or electrical contrivances, for the *cure* of conditions dependent upon degenerated nerves and cells is at best problematic. We know that all degrees of regeneration do take place, but whether or not this regeneration is effected by drug action is a matter of speculation, purely. Treatment of beriberi is symptomatic, generally speaking, because our ignorance of the causative organism precludes any specific medication.

Although practically all of the fulminating cases die, we endeavor, nevertheless, to apply the most rational measures we know of. In these cardiac-crisis cases Gerrard recommends emesis, hypodermatic injections of heart stimulants, lavage of the stomach with boracic acid solutions, normal saline solution by enemata or by hypodermoclysis, inhalations of amyl nitrite (for cyanosis) alternating with oxygen (if available), venesection for acute dilatation of the heart, and morphine by needle for the anguishing pain.

In the nonfulminating acute cases there is more chance for drug action and most of the measures just named are applicable. Stomach-washing with sterile water, or with a very weak solution of formalin, with a view to destroying and removing the microorganisms at the pyloric end of the stomach and duodenum, is rational practice. In this variety of beriberi, venesection for an actually dilated heart will not be as frequently indicated, the cardiac symptoms generally being less urgent. Strophanthus and digitalis are the best drugs to combat the usual heart disturbance, with nitroglycerine in full doses, or amyl nitrite, in reserve for urgent heart conditions as they may occur. If bleeding is required eight or ten ounces of blood should be withdrawn. Manson advises opening the external jugular vein, if blood will not flow from the arm. For vomiting and hiccough, sinapisms over the stomach, and sedatives are indicated. A saline purgative, repeated as required, should be given early in these cases. Effusions into the pericardium or pleural cavities are to be suspected and when present should be aspirated promptly. The pericardium may be tapped close to the left border of the sternum in the fourth or fifth

interspace, or it may be entered through a trephine opening in the middle of the sternum at the same height. In either case wounding the internal mammary artery is to be guarded against. The surgical procedure of approach through the sternum, undertaken with due appreciation of asepsis and surgical responsibility, seems to me to be the preferable operation in these cases. The presence of pericardial effusion, while very common in beriberi, should be reasonably assured before operation is undertaken. Pleural effusions are evacuated in the ordinary way.

The treatment of the great group of subacute cases, and residual paralysis cases, will call for less direct symptomatic medication and more tonic and supportant medication, hyperalimentation and the correction of anemia.

Important for such cases as are but partially disabled, especially those with heart disturbance, is the insistence upon rest in bed. Massage and the indirect induced (farradic) electric current are indicated for muscular atrophy as soon as anesthesia and numbness occur. Bandaging of the limbs, for edema, and the application of splints or elastic devices to prevent or overcome contractures, foot drop, etc., are useful and, at least, serve to prevent deformity.

Bed sores, which are apt to occur in bed-ridden cases, especially cases with edema, are to be treated as when they occur in any other disease. Neuritis often calls for anodyne treatment and few drugs less powerful than morphine suffice to assuage the pains or to give any degree of comfort in severe cases.

Cramps of the limbs call for friction with stimulating or anodyne liniments, change of posture, application of heat, or rarely, chloroform inhalations. In the recurring or relapsing cases especially, permanent removal from the place where infection occurred is imperative. These cases are often benefited by an ocean trip. The indications for hyperalimentation and tissue-building and for blood constructive treatment are plain, in all cases which survive the acute stages of the disease. Iron is perhaps the most reliable drug, in conjunction with all the usual tonics (except strychnine). Strychnine seems to be contraindicated on account of its stimulating action upon the cardiac motor ganglia and the excitability of the

sensory nerves and terminals. Feeding, especially with the nitrogenous articles of food, and administering an abundance of pure water to replace the losses from edema, are important in the extreme, and special attention should be paid to the activity of the digestive and excretory organs.

CHAPTER III.

PLAGUE.

Synomyms. Pest; Pestis Bubonica; Bubonic Plague; Oriental Plague; Levantine Plague.

Definition. Plague, as modernly understood, is an acute specific, epidemic, infectious and highly fatal disease caused by a micro-organism, now well known and recognized, the *bacillus pestis.* It is a disease which occurs in many of the lower animals and birds, as well as in man, and by some recent observers it is considered, principally and primarily, an epizoötic disease capable of direct or mediate transference to human beings.

The causative organism invades many of the tissues, the blood, the secretions, and excretions. The disease is infectious, inoculable and contagious and may be acquired by ingestion or by inhalation of plague bacilli and possibly in other ways. It is characterized clinically by fever, by lymphatic glandular inflammation and swelling, and by a rapid course. Bubo formation occurs in most of the cases, the groins, axillæ and neck being the most frequent sites of the buboes.

Clinically the human disease is divided into three varieties, named in the order of their frequency: *Bubonic plague*, *septicemic plague* and *pneumonic plague.* These three varieties might be designated glandular, circulatory and respiratory plague, and thus indicate the various systems of the human body in which the disease presents its most obvious symptoms. The fact that these distinctions are, in a sense, artificial ones, and that they only indicate localized manifestations of the same disease, should not be lost sight of. This classification is chiefly valuable from a diagnostic point of view. As in most other diseases, atypical cases and extremely mild infections occur, presenting departures from the clinical picture to be described. The terms *pestis minor* and *major* indi-

cate mildness or severity, simply; the terms pestis *ambulans* and larval or abortive plague have also been used to designate mild plague and pestis *siderans* and pestis *fulminans* are terms which have been applied to certain severe cases of pestis major.

Facts of Geography and History. History discloses the fact that from pre-Biblical times epidemics which were almost certainly bubonic plague have occurred; but it is certainly true that every plague of antiquity was not bubonic plague. Literature upon this subject is most fascinating but leads us to few definite conclusions except that bubonic pest, or plague, is truly an ancient

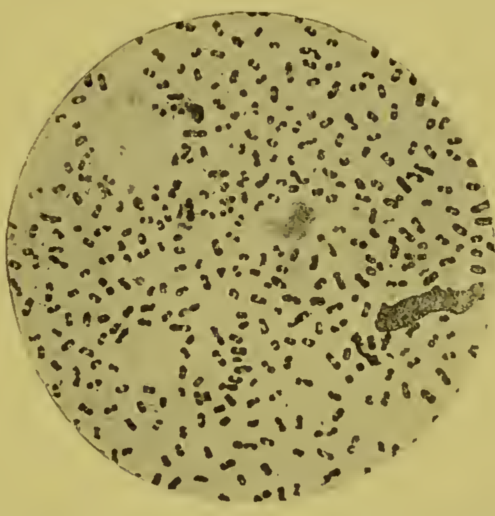


Fig. 21.—Bacillus of Bubonic Plague (Yersin). (From Williams' Bacteriology.)

disease. Apparently the first authentic pandemic of the Christian era began in Egypt in the sixth century, extending thence to Constantinople and Europe, and later to the British Isles, including Ireland. From the seventh century to the time of the Crusades there were many local outbreaks, with periods of quiescence, lasting for a century at a time. The Crusaders spread the disease, in the eleventh and twelfth centuries, through Europe, on their return from the Holy Land, and it ravaged the whole of Europe from the eleventh to the fourteenth centuries, culminating in the second and most terrific pandemic of history, the "Black

Death" of Europe and England of the Middle Ages. Through the fifteenth, sixteenth and seventeenth centuries history presents accounts of the more or less interrupted prevalence of plague in Britain and Europe, especially in London, Paris and the great population centres. Then comes a remarkable disappearance of the disease in Western Europe at the close of the seventeenth century, and a century, the eighteenth, with comparatively few epidemic outbreaks. The nineteenth century found plague lingering in European and Asiatic Turkey and in Egypt, from all of which localities it practically disappeared about 1850.

At the present time there exists a pandemic of plague in the Eastern hemisphere which has been growing and becoming diffused throughout the Far East for ten or fifteen years past, and which has recently threatened the Western American seaboard and even gained a short-lived foothold in the United States. Its present-day importance is indicated by the appalling magnitude of its death rate in India, which for the year 1903 was officially reported to be 847,030, but which, doubtless, actually exceeded 1,000,000 persons. Between 1900 and the present time epidemics of more or less gravity have occurred in China, Japan, the Philippine Islands, Australia, the Hawaiian Islands, Mexico, Brazil, Peru, Cape Colony, South Africa, Glasgow, Scotland, Egypt, Suez and Mauritius, and there can be no question that cases of bubonic plague occurred in San Francisco in the United States. It has therefore encircled the globe, following the paths of commerce, and its importation is a real and ever present danger to every country engaged in international commerce. Nowhere else in the world, however, do the epidemic conditions approach those which have so recently prevailed in India and which continue to prevail in an intense degree.

The reported deaths from plague in India, in 1904, reach the grand total of 1,040,429 indicating an increase rather than a decrease over the official figures for 1903. (Treatise on Plague, W. J. Simpson—1905.)

In April, 1905, the official report of plague deaths in India during one week reached 56,732. If this rate were maintained it would

mean an annual loss of nearly 3,000,000 lives from the plague. Surely the high-water mark of fatality for this dreadful epidemic has been reached.

Etiology and Prophylaxis. The bacillus pestis was discovered by Kitasato in the Hong-kong epidemic in 1894, and also by Yersin, working independently in the same epidemic, at about the same time. It is a short, thick bacillus measuring from 0.8 to 2 microns in length and from 0.4 to 0.8 of a micron in thickness. It has been described also as a cocco-bacillus and has rounded ends. A capsule can usually be made out and the stained organism resembles a diplococcus, by reason of the more intense bipolar staining, the intermediate portion of the rod taking the stain faintly. (See the section on laboratory detection at the close of the chapter.) These bacilli are found in pure culture in buboes, or they may be associated with pyogenic streptococci and staphylococci. The bacilli are also present in great profusion in the viscera, liver, spleen, intestines, lungs, kidneys, urine and feces and in the sputum and blood in pneumonic and septicemic cases. Experimentation has recently shown that the following animals and birds may contract the disease: Rats, mice, cats, dogs, monkeys, calves, pigs, sheep, ducks, geese, turkeys, and pigeons. Most of them may contract it by eating materials containing plague bacilli and all of them, when infected, excrete and distribute plague bacilli in their feces and urine. Insects, such as flies, may also transport plague bacilli and it has been proved that fleas which infest plague infected rats also bite human beings, although the actual production of plague in man by this means remains to be proven. Rats are admittedly the most active carriers of plague infection in time of epidemic, and this fact is recognized by sanitarians generally, in their efforts to exclude the disease or to eradicate it from cities and villages.

The bacillus pestis may gain entrance to the human body through several channels. It may enter the lymphatic spaces directly through the skin, and this is the most common conception as to the usual route of entrance. It is one which explains rather satisfactorily the occurrence of superficial buboes in lym-

phatic glands supposed to be nearest to the point of entrance in the skin.

As a matter of fact, however, it is not often possible to trace the route backwards, from the primary bubo to the point of entrance in the skin. This may perhaps be due to the microscopic character of the skin lesion, through which it is as easy for the bacilli to pass, theoretically at least, as through a gross lesion. On the other hand there are many instances of inoculation at distant parts of the body from the primary bubo, as for example, an inoculation scratch in the left forearm followed by a left femoral bubo. In such a case the inoculation probably occurs directly into the blood current, and the bacilli reach the lymphatic system indirectly and become localized in a distant group of lymphatic glands. It has been established that infection through the skin may occur without subsequent irritation at the point of inoculation. Abrasions of the mucous membranes, as will be pointed out, permit plague bacilli to pass into the lymphatic and circulatory systems beneath, and it has also been experimentally shown that the organism may penetrate mucous membranes in which no lesions, or at least no perceptible lesions, exist. These facts explain the manner in which respiratory plague and ingestive infections (through the alimentary tract) occur.

The nostrils, pharynx, and tonsils are sometimes the sites of entrance for the bacilli. Vomitus and menstrual flow from plague patients have also been known to serve as media of direct infection to others.

Many recently demonstrated and important facts are to be credited to the English commissioners designated by the British Colonial Office to investigate the causes and continuance of plague in Hong-kong, Cape Colony, and elsewhere, and the recent reports of W. J. Simpson, M.D., F.R.C.P., are exhaustive and highly enlightening. Among the important facts brought out, which have direct bearing upon the distribution of the disease, is the one that many fowls suffering from plague will be apparently well, feeding and going about, even with high febrile temperatures, for from thirty to fifty days after contracting the disease.

Pigs, especially, have been shown to resist the fatal effects of plague for a long time, presenting, meanwhile, the appearance of health and at the same time scattering the plague bacilli widely, in their feces and urine. The possibilities of the extension and continuance of epidemics, by these and other animals used for

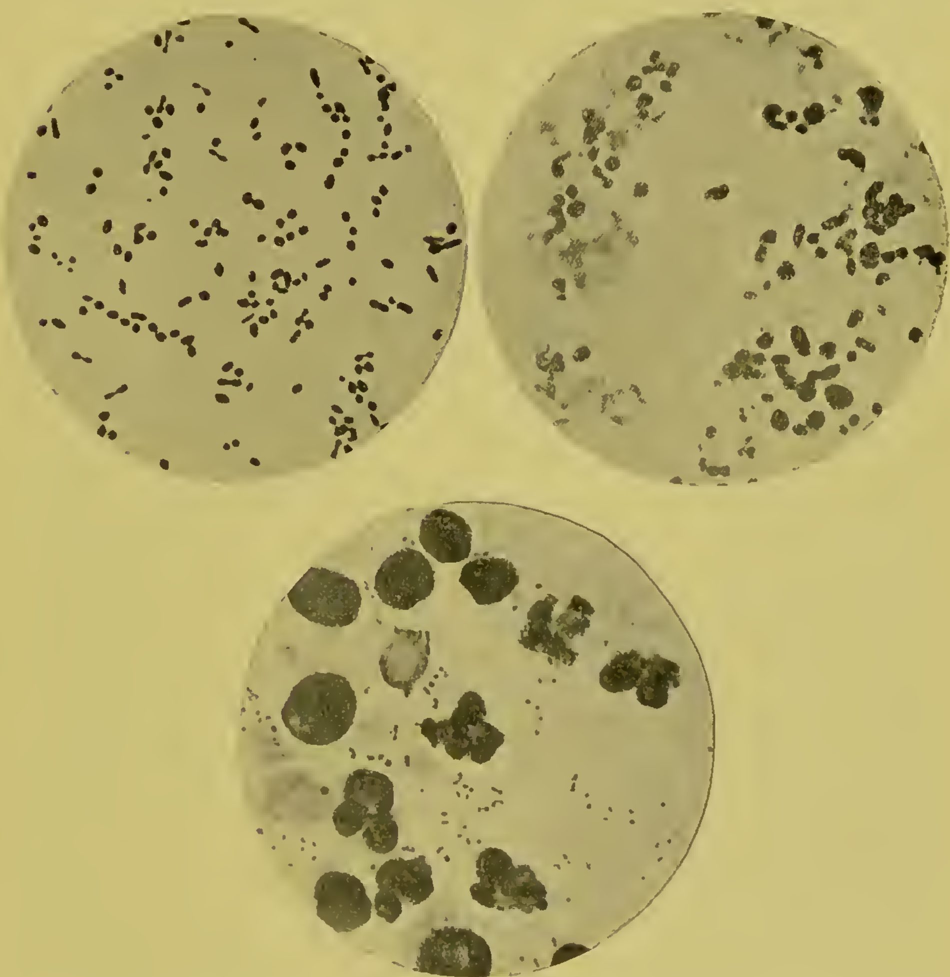


Fig. 22.—Showing cultures and involution forms of bacillus pestis and bubonic pus containing the bacilli. (Reproduced, by kind permission, from Simpson's Treatise on Plague, 1905.)

food, and in various other ways disclosed by the work of these commissions, are very large and the importance of this knowledge is apparent in its relation to prophylaxis. Animals fed upon food containing plague bacilli may acquire the disease through the

stomach and intestine (although this is probably not the usual way), and in like manner, the flesh of plague-infected pork or fowls, especially in an uncooked or partly cooked state, may be the infecting material in human plague. It hardly need be stated that the importation of pork and fowls from plague-infested localities should be interdicted by law and that the law should be rigorously enforced.

Some of the important facts established by observations of epidemics, and by experiments which cannot be detailed here, are as follows: The virulence of the plague bacillus varies and is susceptible of attenuation or intensification. Ingestive infection of animals usually gives rise to the septicemic variety of plague. The disease is contagious but less so than scarlet fever, smallpox, or measles. Age, sex, occupation, altitude, temperature and character of the soil do not particularly affect the occurrence or extension of plague. It follows the routes of commerce in the same manner that cholera does, traveling less rapidly than that disease, however, and progressing more by place infection than by direct communication between persons. Plague is transportable, the organism living within human or animal bodies, and outside of them, upon contaminated articles, for variable lengths of time. It may be carried by human beings who are in the incubation or invasion stage of the disease, from an infected to a healthful locality, and the same is true concerning animals; and it may even be conveyed from one place to another by a person who is himself free from the disease.

This conveyance by the healthy is most likely through the medium of infected clothing. There are plenty of instances of record to support the belief in conveyance and distribution of plague by infected clothes or effects, either personally conveyed or shipped, and frequently the disease is conveyed over long distances in ships, in this manner. This possibility, and those of infected rat and food-conveyance, in reality constitute greater dangers than a case of the human disease itself, which may be recognized and radically dealt with. The recorded and authentic instances of infection conveyed by cargoes and rats, are more than a few.

Sick rats are also liable to remain in crates or bales of merchandise, and may thus be shipped great distances by rail or water, or both, and may infect the rats at the destination point, either inland or sea-port, even if dying in transit. In this connection it is a most suggestive fact that epidemic plague among rats often precedes the appearance of human pest in a new plague-infected centre or town. These observations concerning rats probably apply to mice with equal force, these animals being susceptible and suffering from plague.

Among the means proposed for destroying rats in a wholesale manner is the dissemination among them of an epizoötic disease fatal to rats but harmless for human beings and domestic animals. J. Danysz isolated a bacillus from field mice suffering from an epidemic, and experiments looking to the wholesale spreading of the disease among the rats in different towns, by setting free infected rats, have been conducted, with indifferent success only, however.

The epidemic produced among rats in this manner is not fatal enough to completely destroy them. Feeding experiments have been more successful. Experimentally, the disease produced by feeding rats with Danysz bacilli destroys only about 33⅓ percent. of the animals infected. It is claimed, however, that the bacillus is capable of developing increased virulency by culture, and in Cape Town, South Africa, in 1901, and in Odessa, Russia, in 1902, the use of this method was followed by a very decided decrease in the number of rats. In Odessa the results were so successful that after some weeks of operation of the method, rats were practically unobtainable in the city, even when rewards were offered for them. It was found that small pieces of bread, soaked in alkaline bouillon cultures of the Danysz bacillus, and distributed nightly, are the most successful vehicles of the disease for rats. Thousands of pieces should be distributed nightly. The incubation period of the disease in rats is about eight days.

When rats suffer from bubonic plague the disease is of the septicemic variety, and usually of an acute type, although a sub-acute or chronic type has been recognized. This latter variety

of the disease, in rats, is the form of plague noted in rats caught alive during the interruptions in epidemic conditions of the human disease. The acute septicemic plague of rats is an hemorrhagic disease, as is septicemic plague in man.

Much of the foregoing bears directly upon, and indicates, procedures of prophylaxis. To summarize: We may divide our efforts

Fig. 23.—Axillary Bubo. (Reproduced, by kind permission, from Simpson's Treatise on Plague, 1905.)

of prevention into those for the community and those for the individual. For the community we strive to prevent the introduction of plague, and, in the event of its presence to prevent its spread. Quarantine, applied to persons, goods and animals, cannot be too strictly carried out.

Persons with the disease, or the history of exposure to it,

should be isolated or detained for observation; goods from infected ports, susceptible of harboring plague bacilli or rats, should be subjected to *efficient* disinfection; and animals, living or dead, not entirely above suspicion, should be excluded or destroyed. Whenever quarantine measures of this kind are attempted there will always arise bitter protest on the part of the public, or at least a portion of the public, on the ground of interference with commerce and the hardships and damage to the business of the community or state. The officers to whom the enforcement of the quarantine is entrusted must be men of high purposes and of conspicuous moral courage, and behind them should be the power of the national government. Nothing less powerful than the national authority will be satisfactory backing at such times. The fumigation of the cargoes of arriving ships, if from infected or suspected ports, and the destruction of rats, both aboard ships and ashore, should be insisted upon, and in towns the streets, sewers and buildings, both public and private, should be subject to sanitary inspections and treatment, by authorized officials with ample power and funds to correct abuses.

In Hong-kong and Manila the expedient of offering a small sum for every rat delivered, dead or alive, to the health authorities, has been found to be an extremely effective way of arousing the natives to the wholesale destruction of these vermin. Accompanying each rat, when delivered to the health department, there should be a record card indicating the address of the premises in which the rat was captured.

All the rats should be examined for evidences of plague and, when present, the premises in which the rat was captured should be thoroughly disinfected and its inhabitants strictly inspected for signs of human plague.

To prevent the spread of the disease, every suspicious case should be isolated and observed. In the case of every suspicious death, an autopsy should be made, and the disposal of the dead should receive careful attention. If cremation be impracticable, interment should be made in quick-lime, after saturation of the clothing and body in some disinfectant solution. Disinfection,

rationally applied, does not mean the wasteful and extravagant scattering about of expensive chemicals. Under capable supervision it may be effective, far-reaching and economical. The greatest effort, however, should be directed to secure the observation of sanitary laws, particularly in regard to cleanliness, the use of latrines, and the preparation and care of foodstuffs.

Concerning the manufacture of the Japanese prophylactic serum of Kitasato, for bubonic plague, prepared at the Imperial laboratories in Tokio, Lieutenant Calvert, United States Army, who visited the Japanese laboratories during the plague epidemic in Manila in 1900, for the Manila Board of Health, writes as follows. (Report of the Surgeon-General, United States Army, for 1900.)

"A brief description of the preparation of plague antitoxin will be given. Large quantities of sterile cultures of the plague bacilli are repeatedly injected into the horse at intervals of two weeks. After from eight to twelve inoculations a small quantity of serum is prepared for experimentally testing its strength. When larger quantities of serum are desired, from 2,000 to 2,500 c.c. of blood are withdrawn from the jugular vein. The blood is then whipped, centrifugalized, and the clear serum drawn off and made a one-half percent. solution of carbolic acid. It is then ready for use. Three days after blood is withdrawn from an animal, another inoculation is made, and two weeks later blood may be again withdrawn. This cycle may be repeated as often as desired.

"Thus far serum has been prepared which has a protective power, but at present is not successfully used for therapeutic purposes. It is claimed by some that when used in very large quantities the serum reduces to some extent the mortality. Serum mixed with equal parts of sterile cultures is sometimes used to protect exposed persons. From 0.6 to 0.8 c.c. of this mixture is used for the first injection. The serum is supposed to give immediate protection while the toxin in the sterile culture is being converted into antitoxin. After the reaction has subsided from 0.8 to 1 c.c. of sterile culture is used for the second injection. Thus far

plague antitoxin sufficiently strong for therapeutic use has not been made or is not generally known."

The prophylactic inoculations suggested by Haffkine, in India, and practised in epidemics there and in China, are made with bouillon cultures of pest bacilli, which have been subjected to a degree of heat sufficient to kill the organisms without destroying the toxin. These inoculations have been practised with moderate success only, the reaction following the hypodermatic injections being quite severe in many cases. Moreover, the protection does not occur for forty-eight hours after inoculation.

It has also been used in the treatment of the disease itself and a marked reduction of the mortality has been reported in groups of cases treated with it. The Indian Plague Commission concluded that: "1. Inoculation sensibly diminishes the incidence of plague attacks on the inoculated population but the protection which is afforded against attack is not absolute. 2. Inoculation greatly diminishes the plague death-rate among the inoculated population. This is due not only to the fact that the rate of attack is diminished, but also to the fact that the fatality of attacks is diminished. 3. Inoculation does not appear to confer any great degree of protection within the first few days after the operation has been performed." The principal dangers and obstacles attending its use seem to reside in the difficulties of standardizing the product, its liability to contamination with other bacteria (as for example, the tetanus bacillus), the unwillingness of the populace to receive the inoculations, and the uncertainty of its action.

Galeotti and Lustig, of Florence, have also prepared a prophylactic nucleo-proteid from agar plate cultures of pest bacilli, which is in the form of a powder, soluble in a 0.5 percent. solution of carbonate of soda, and hypodermatically administered in doses of three milligrams. The dangers of contamination are minimized in its preparation and the sterility of the preparation, and the definite quantity used, recommend it as a substitute for the Haffkine toxin, but evidence of its value in epidemics of human plague are wanting as yet. It appears to be protective for monkeys, rats, rabbits, and guinea pigs.

We will consider the use of antitoxic serum under the head of treatment. An attack of the disease itself confers a very uncertain immunity. There is no lack of cases on record in which an individual has suffered two attacks in the same year, and cases of individuals incurring second attacks of plague in repeated epidemics are not rare.

The personal side of the problem of prophylaxis, or the self-protective measures for the physicians, nurses, attendants, members of families, and servants of plague patients, demands more specific actions and endeavors. These include personal cleanliness of the body, and disinfection of the hands, face and exposed parts, frequently, and invariably after contact with the plague patients, their sputa, excreta, clothing and bedding, and also after contact with those under suspicion. Hot water and soap (a germicidal soap by preference) and solutions of disinfectants, such as a 0.5 percent. carbolic acid solution, or a 1:2000 bichloride of mercury solution, should be used and the face and hair should not be neglected. Open wounds, cuts, abrasions of the skin, "hangnails," etc., should receive protective applications of collodion, or some other water-proof dressing. The feet should be protected and barefooted servants, the customary kind in the Philippines, should not be countenanced in the vicinity of plague patients. The destruction by fire of all dressings from buboes, and the disinfection, with solutions of chloride of lime or carbolic acid, of all excreta, including the urine, should be imperatively required. Attendants should wear overgarments or gowns, wrung out and kept moist in a solution of bichloide of mercury 1:1000, whenever in contact with the patient or in the room with him. Hot foods only should be taken; the windows of the apartment should be screeened and all food should be protected from exposure to flies, ants, rats, etc. In the presence of cases of pneumonic plague, attendants will do well to protect their mouths, nostrils, and eyes from the bacilli coughed up by the patient, by wearing cheesecloth masks or veils wrung out in a germicidal solution. There are on record many cases of infection by the inspiration of coughed up or expectorated material, and there are even authentic cases of conjunctival infection

followed by true bubonic plague, acquired in this manner. According to Simpson (p. 256, "Treatise on Plague"), such a case occurred in 1897 in the person of a Bombay nurse at the Parel Hospital, a parotid bubo following the conjunctival infection. The case terminated fatally. A slight abrasion of the exposed mucous membrane, anywhere, is an open gateway for plague bacillus infection. In Manila the disease was shown to be communicated through sexual intercourse.

Fig. 24.—Inguinal Bubo. (Reproduced, by kind permission, from Simpson's Treatise on Plague, 1905.)

Pathology and Diagnosis. In considering the pathology of pest we will first consider the most distinctive manifestation of the disease, the bubo. For convenience and a better understanding of the phenomena of bubo formation, rather than for clinical reasons, buboes have been grouped into classes known as primary and secondary, and the first class has again been subdivided into those of the first and second orders. Primary buboes are those which occur in the lymphatic glands nearest to the points of en-

trance of the pest bacilli, and are present in the cases in which the lymphatic systems are directly infected, the great majority of all cases. Secondary buboes are those in which certain lymphatic glands are secondarily infected through the blood current. They may, therefore, occur in cases in which either the lymphatic or circulatory systems receive the initial infection. The primary bubo of the first order, is the first lymphatic gland affected and it usually shows the most intense pathologic changes. The primary bubo of the second order, is single or multiple and occurs in the same chain of lymphatic glands in which the primary first-order bubo occurs, and close to it. The distinction is not striking clinically.

The primary first-order bubo represents a swollen gland, more or less fixed by infiltration of the surrounding tissues and associated with a varying amount of overlying edema and redness of the skin. The serous exudate giving rise to the edema is of gelatinous consistency and straw-yellow in color.

When incised a thin fluid of the same color exudes from the tissues. This fluid contains leucocytes, plague bacilli and some red blood cells. Engorged blood vessels, with small hemorrhages, are present in the tissues. According to the amount of exudate present the normal contour of the skin is preserved or obliterated.

Primary second-order buboes are smaller, more movable and without the surrounding edema and infiltration of those of the first order, unless situated very close to the latter. The lymph vessels are distended, and hemorrhages within and without the glands are observed. Under the microscope, bubonic glands show coagulation necrosis, white and red blood cells, and masses of pest bacilli, either alone or in association with other bacteria. Pus is not usually present.

Secondary buboes are similar to primary ones and show the same microscopic changes.

Buboes are more common in the femoral, inguinal, axillary and cervical regions, in the order of frequency given. Primary first-order buboes occur from the first to the fourth day of the disease, and the second-order buboes very shortly after. The ten-

dency is towards suppuration, which may occur at the end of the first week, or even earlier. After either spontaneous opening or incision, healing is usually tardy. Secondary buboes are less likely to suppurate. Hemorrhages into and under the skin sometimes occur, the subcutaneous hemorrhages being either punctate or extensive. They vary in color from red to black, and the larger ones resemble bruises. These hemorrhagic tissues contain many

Fig. 25.—Plague Carbuncle. (Reproduced, by kind permission, from Simpson's Treatise on Plague, 1905.)

bacilli. So-called plague carbuncles sometimes occur, probably as metastatic "buboes" of the skin. They develop rapidly, as coalescing small vesicles, appearing over a spot of discoloration of the skin. A large vesicle results which ruptures, discharging bloody fluid containing pure or mixed cultures of plague bacilli, leaving an ulcer with indurated, sharply defined edges. Extensive edema and nearby lymphatic swellings occur.

Generally speaking, the other pathologic changes noted in

plague are evidences of hyperemia and congestion, hemorrhage, and fatty and parenchymatous degenerative changes in organs. A general diffusion of plague bacilli, throughout all the tissues of the body, occurs in the cases which become systemic.

We have already referred to the *lymphatic* and *integumentary systems*. In the *circulatory system* there are evidences of dilated heart, pericardial congestion, fatty degeneration of the heart muscle and hemorrhagic areas in the tissues. These hemorrhages extend to the tissues of the walls of the veins, in some cases, but the arteries usually escape. The *blood* itself shows no distinctive changes, except an increase of blood platelets and a leucocytosis, sometimes as high as 50,000, the polymorphonuclear white cells being especially increased.

Plague bacilli are present and demonstrable in the blood in varying numbers, according to the variety, stage and extent of the disease. They are not usually to be made out earlier than the third day, unless the case is of the septicemic variety from the outset.

The *liver*, *spleen* and *kidneys* all show hemorrhages and fatty degeneration.

Both spleen and liver are enlarged, the spleen often to three or four times its normal volume and the liver moderately. In the *digestive system* we encounter varying grades of congestion and hyperemia of the mucosa of the mouth and tongue, tonsils and pharynx. The mucosa of the stomach and intestine shows the same changes and may also present hemorrhages of greater or less extent. The mesenteric glands are swollen and may be the seats of buboes. The iliac glands may also become bubonic.

The *muscles* and *bones* show no distinctive changes.

In the *respiratory tract* the larynx, trachea, bronchi, lungs and pleuræ may be inflamed, edematous or hemorrhagic, and associated lymphatic glands in the mediastinum and at the bases of the lungs may be inflamed, or become the sites of secondary buboes. Bronchitis, pleuritis (with or without effusion), broncho-pneumonia, or lobar pneumonia may be present in cases of respiratory or pneumonic plague.

Diagnosis. The rapid diagnosis of plague is often of extreme importance, especially in the early days of an epidemic, or when the importation of the disease into a plague-free community is threatened.

Typical bubonic cases, occurring in the midst of an epidemic, are readily recognized from their clinical appearance but sporadic cases departing from the ordinary types, may often defeat conventional diagnostic attempts. In such event, positive diagnosis is only possible after a bacteriological investigation which, fortunately, is usually easy and decisive. The procedures will be described in the section on laboratory detection.

Blood from the patient, either for direct examination or for culture, the fluid from edematous tissues about the buboes, smears from the contents of open or unopened buboes, or sputum from pneumonic cases, may be used. Larger amounts of blood for inoculating rats and guinea pigs may be obtained from the patient by wet cupping. It will usually be easy to obtain cultures, or to demonstrate the organism without culture, from the cadaver.

Serum diagnosis, based upon the agglutinating properties developed in the blood of plague cases by the presence of pest bacilli, may sometimes be utilized. Owing to the inconstancy of this phenomenon (it occurs in less than half the cases), it is of indifferent value for diagnosis. To produce the reaction: Dilute the serum of the patient with normal salt solution to a proportion of 1:3 and then add a particle of an active bouillon culture of plague bacilli. The agglutination or clumping phenomenon resembles that of enteric fever, except that it is much less constant than the reaction for typhoid fever and consequently far less valuable for diagnostic purposes. A negative result from the application of this test in individuals suspected of plague infections will, therefore, be of little value as indicating freedom from the disease.

Considering the clinical diagnosis of plague, without microscopic recourse, we should remember that fever in association with adenitis, is to be looked upon as a suspicious circumstance if it occurs in the presence of an epidemic of plague. The sudden onset

and the rapid development of fever, with an extreme degree of prostration, a prostration more profound than that of nearly every other disease, are significant and diagnostic if they occur in association with one or more buboes. Mild infections with plague bacilli and the formation of buboes are apt to be mistaken for venereal infections. Here, the history and a careful inspection of the patient should clear up the matter. Lymphangitis and adenitis due to staphylococcic or streptococcic wound infections, may simulate bubonic plague. The usual infected wound, the localization of swelling and tenderness, and especially the prompt response to surgical treatment and antiseptic dressings, should throw light on these cases. Mumps and tonsillitis may both simulate bubonic plague as may dengue with lymphatic swelling, also. The clinical diagnosis of non-bubonic cases of plague, the septicemic and the pneumonic, may be more difficult. Cases of plague without superficial bubo, and with involvement of mesenteric glands in the cecal region, may suggest appendicitis. Cases of respiratory plague may be mistaken for cases of bronchitis or broncho-pneumonia of the ordinary varieties. Typhoid fever and malarial fever have both been confounded with plague. The less sudden onset of typhoid and the Widal serum test, and the presence of hemamebas and melanemia in malarial fever, should prevent mistakes of this kind. Speaking generally, the history of each case, the presence or absence of venereal sores or of infected wounds, the blood tests and the clinical picture of plague, remembering its variations, should all be considered in making up a diagnosis.

In advanced cases, even when plague bacilli are not demonstrable in the blood, an increased number of blood platelets and a polymorphonuclear leucocytosis is a suggestive circumstance, and it may also serve to clear up any question of enteric or malarial fever which may be entertained.

Illustrative of the difficulties of diagnosis from symptoms alone, in isolated cases or in the early mild or abortive cases of epidemic plague, is the following case which I observed in the Philippines at Naic, Luzon, in September, 1901. This case was reported in

the Philadelphia Medical Journal of April 5, 1902, and was printed in the annual report of the Surgeon-General, United States Army, for 1902, from which I quote it. It should probably be classified with the mild bubonic cases. The case also illustrates the necessity for early and microscopic diagnosis, in order that appropriate quarantine and isolation may be instituted.

"During the night of September 12 a native scout appeared at this hospital complaining of severe, cramp-like pains in the calves of both legs. He was given chloroform liniment, as an application, by the hospital steward and returned to his quarters, appearing the following morning, September 13, at sick call with a temperature of 103° F. Examination revealed a well-developed left femoral bubo of the size of a small lime, and as no venereal lesion was found he was immediately isolated.

"Owing to his lack of knowledge of English and Spanish it was difficult to elicit a complete history, but by means of an interpreter the following facts were gathered: Julian Gonzales, about twenty years old, native scout, quartered with Company I, Fourth Infantry, returned with six other scouts from Magallanes, September 9 in good health. He denied having chills, fever, or symptoms of malarial disease or other recent illness.

"In the absence of a microscope, malaria could not be excluded. Quinine was administered, and was continued throughout the illness by mouth and needle. Bowels and kidneys performed their functions normally. The bubo increased in size during the first twenty-four hours, attaining a large size. The skin was quite tense, and the bubo moderately tender. At the end of twenty-four hours the bubo began to diminish in size and consistence, but showed no signs of suppuration. It has now almost entirely disappeared. A few inguinal glands and one cervical gland of the same side became slightly swollen, but there was no other manifestation of glandular enlargement. Upon the fifth day the temperature dropped to 99° F., but the afternoon temperature of the same day was 103° F. Upon the morning of the sixth day the temperature was slightly subnormal.

"District, department, and division chief surgeons were notified

by telegram, and the civil health authorities in Manila wired to send an inspector.

"Every precaution was taken to prevent contagion. The quarters in which the case occurred were thoroughly disinfected, and the patient was isolated in a tent in the middle of a large field, attended by a native scout, and visited by me three times a day. The commanding officer furnished a guard to prevent unauthorized communication with the patient.

"In the absence of a microscopical diagnosis, I inclined to the opinion that the case was one of sporadic plague for the following reasons:

"1. The appearance of a femoral bubo without venereal lesion or other nearby skin lesion, coincident with acute febrile symptoms is most unusual in cases of malarial disease. In recent experience of two thousand or more cases of malarial disease I have not met with such a combination of symptoms.

"2. The onset and progress of the case suggested an acute infectious disease.

"3. The recent occurrence in this town of five cases of bubonic plague, three fatal, readily accounted for the origin of the case, the infected buildings still remaining. It is now beyond the power and province of the medical officer to destroy these buildings, the town being under civil rule.

"4. The temperature curve might be variously interpreted and was not inconsistent with plague.

"September 18: Upon the afternoon of September 17, Dr. J. F. Halsell, representing the Manila Board of Health, made a blood examination of the case under suspicion. No malarial parasites nor pigment were discovered, but plague bacilli were found in several specimens examined, making positive the diagnosis of bubonic plague.

"September 19: Case is now convalescent, but under strict quarantine."

The thermograph of the case appears on page 111.

In this case blood cultures were not necessary, the blood films being stained with methyl blue after fixation. No doubt the tissues

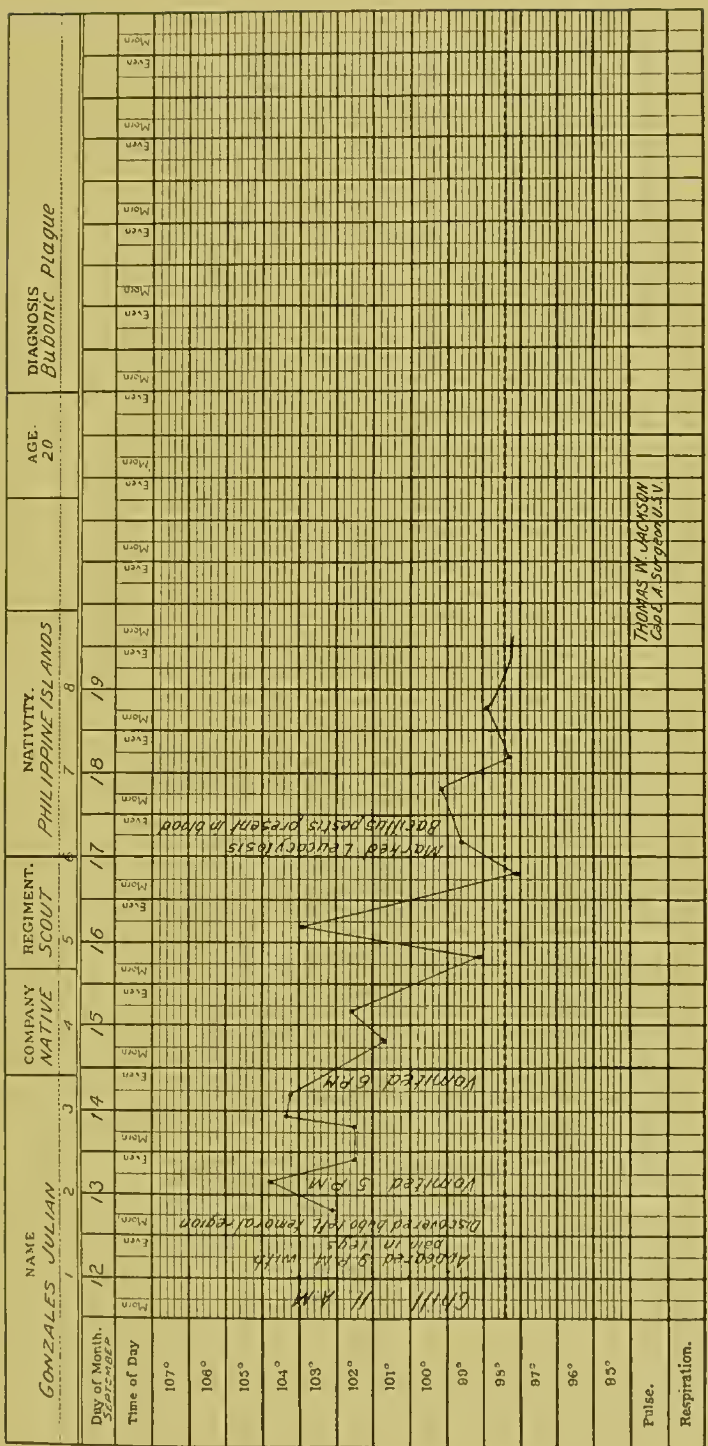

NAME GONZALES JULIAN
COMPANY NATIVE
REGIMENT. SCOUT
NATIVITY. PHILIPPINE ISLANDS
AGE. 20
DIAGNOSIS Bubonic Plague
Day of Month. SEPTEMBER
Time of Day
Morn
Even
12
13
14
15
16
17
18
19
107°
106°
105°
104°
103°
102°
101°
100°
99°
98°
97°
96°
95°
Pulse.
Respiration.
Chill 11 A.M
Admitted 9 P.M. with pain in legs
Discovered bubo left femoral region
Vomited 5 P.M
Vomited 6 P.M
Marked Leucocytosis
Bacillus pestis present in blood
THOMAS W. JACKSON
Capt. A. Surgeon U.S.V.

Fig. 26.

about the bubo, if aspirated with a hypodermic syringe, would have yielded the plague bacilli abundantly.

The following tabulation is from the known cases of plague which occurred in this town (Naic) during 1901.

NATIONALITY.	AMERICANS.	FILIPINOS.	CHINESE.	COMBINED.
Total Number Cases.	1	3	2	6
Fatal Cases.	1	2	0	3
Percent Mortality.	100	$66\frac{2}{3}$	0	50
Cases With Suppurative Buboes.	0	2	2	4
Cases Without Suppurative Buboes.	1	1	0	2

Symptoms and Treatment. We will first describe the most prevalent form of plague, the bubonic type of the disease. The stages or periods of incubation are practically alike for all the types, bubonic, septicemic and pneumonic. The incubative stage varies from a few hours, in rare fulminating cases, to ten days, and the average period may be said to be from two to eight days. As long an incubation period as fifteen days has been assigned to the disease by some writers but there seems to be little warrant for this teaching. The *invasion* period is abrupt and promptly ushers in the acute stages of the disease. Both septicemic plague and pneumonic plague are apt to have more intense invasion periods than the bubonic type of the disease. Prodromes are inconstant in all types of plague, and when present consist of vague aching in the limbs, chilliness and loss of appetite.

In glandular (bubonic) plague the invasion period is marked by a sudden onset of fever, by headache of great severity, by aching

in the limbs, and by vertigo. Nausea and vomiting may accompany the onset and a single sharp chill, followed perhaps by irregular ones, may occur. The vertigo may be pronounced and the patient may have a staggering, drunken gait, if he be able to walk at all. When the febrile stage of the disease is established the symptoms rapidly develop. Two conspicuous symptoms are the profound prostration and the peculiar facial expression of the patient. The expression is anxious and pain of an anguishing character is usually reflected in it. The pupils are dilated and the eyes are injected and may be crossed, fixed or staring, and they appear to be sunken in their sockets. The skin is hot and dry and there is considerable itching. Over involved glands it becomes red, tense and edematous. The appearance of hemorrhage, into or beneath the skin, seems to be much more prevalent in some epidemics than in others. The discoloration caused by this occurrence, and the black vomited material of these hemorrhagic cases, seem to have been the occasion for the designation, "The Black Death," applied to the plague pandemic of the Middle Ages. These hemorrhages when present are usually noted late in the course of the disease. The temperature often reaches the highest point within thirty-six hours and 103° F., 104° F., or 105° F. may be attained. The pulse and respiration rates usually correspond with the temperature. The pulse may vary from 90 to 145, and the respiration rate from 30 to 50 per minute. The pulse, however, early loses its volume and becomes thin and dicrotic. The tongue becomes coated with a white fur and later becomes dark brown and swollen, and accumulations of sordes occur upon the teeth. Thirst is a prominent symptom and vomiting and delirium may develop. The voice becomes very weak. If delirium appears, it may be either noisy or quiet in character, and convulsions, or coma, may succeed, according to the extent of the poisoning of brain and nerve centres, by the toxin of the pest bacilli. On the other hand, apathy and the typhoid state may develop without actual delirium. The bubo, which has already been described, may develop within the first thirty-six hours or its appearance may be delayed for two or three days. In the major-

ity of cases the buboes are single but, as has been previously stated, they may be multiple and, if we include the secondary ones, they may be very numerous. Primary buboes vary in size from that of an olive to that of an orange and they are usually very painful, although occasionally pain is slight. Concurrently, there occur in the adjacent tissues the changes which we have considered under the heading of pathology. With the development of the bubo, in a favorable case, the symptoms become more or less localized about it, and a decrease in the severity of the systemic symptoms ensues, which in some cases is almost critical in character. In certain cases a crisis-like change in the systemic symptoms occurs without bubo formation. In either event there is noted improvement in temperature, pulse, respiration, state of skin, mind and faculties, and the thirst and the dry, parched condition of the tongue and mouth disappear.

The buboes reach their greatest size in from one to four days, during which period local pain is very severe, unless the patient be in a comatose state. At maturity this pain abates considerably and may entirely disappear, but if suppuration supervenes the pain persists.

As has been already pointed out, suppuration and spontaneous rupture of the bubo may not occur, suppuration being the usual termination, however. Death may occur at any stage of the disease; either in the first day or two, in cases of septicemic or pneumonic plague, or after a prolonged illness marked by exhausting suppuration and fever, in the bubonic varieties. If convalescence follows the development of the bubo, it may be either slow or rapid, according to circumstances. If the buboes do not suppurate it is apt to be prompt, but if suppuration and spontaneous rupture of the buboes occur, or if incision be performed, the process of sloughing and healing may be a tedious one, marked by various surgical complications and septic intoxication. At any time in an apparently favorable case hemorrhage may occur with fatal result.

During the febrile course of plague the urine may contain a small amount of albumin and partial or complete suppression may occur.

Hyaline casts may be present. The bowels may be constipated or loose, throughout, or in alternation, or they may perform their functions normally. Nausea and vomiting are inconstant and pain in the epigastrium and abdomen may be present and, in fact, is rather a common symptom. Pregnant women almost certainly abort if attacked by plague and the fetus may present both glandular and circulatory evidence of infection. It is difficult to state any average duration for the plague symptoms. When apparently convalescent the patient may show evidences of new localization of the disease, and a new febrile period may succeed.

The usual duration of an uncomplicated case is about a week. Secondary suppurative infections are common. Naturally, complications or relapses in the course of a disease so devitalizing as plague, are most unfortunate occurrences. The prognosis, grave at all times, becomes most unfavorable under such circumstances.

Septicemic plague is a virulent variety of pest, due to the invasion of the blood by the plague bacilli in great numbers. Clinically, there is an absence of bubo formation, but postmortem evidences of general swelling and congestion of all the glands of the body are usually present. The bacilli are readily found in the blood. The characteristic features of septicemic plague are the rapidity in onset, and the intensity of toxemia and attendant nervous symptoms. Profound nervous prostration is evidenced in many ways. Delirium, stupor or extreme restlessness, pallor, involuntary bowel movements, and the algid state may be noted. Epistaxis, hematuria and intestinal hemorrhages, occur in this variety and in case of a few days' duration plague bacilli may be recovered from the urine. An utter absence of reacting power is present in most cases, but in a few instances reaction does occur and the bubonic type of the disease may supervene on the fourth or fifth day, multiple buboes appearing in axillæ, groins or elsewhere; or secondary pneumonia may develop. The temperature after the first stage is passed is low, often remaining at 100° F., or less.

Some mild cases of septicemic plague also occur, and the absence of buboes, and the low temperature, may give rise to diagnostic errors or oversights. Septicemic plague is more fatal than glandular plague.

Pneumonic Plague. The pulmonary variety of plague is characterized by its extreme infectiousness and fatality. In a general way the systemic symptoms described for the bubonic variety are applicable to pneumonic plague, the onset and invasion being similar but somewhat more sudden and rapid than in glandular plague. Ordinarily the pulmonary symptoms develop within the first twenty-four hours, but they may be delayed until the second or third day. In this event diagnosis will be difficult or impossible. When sputum appears, stained smears for microscopic examination can be made, and the disease diagnosed in this manner, an important measure, as a suspicion of influenza may mislead one. If sputum does not appear, as rarely happens, cultural and animal experimentation may be required to establish a diagnosis. A sense of constriction in and across the chest, with rapid and painful breathing, are the earliest pulmonic symptoms. Within a day, a thin sputum, frothy and perhaps blood-streaked, appears and increases in amount, at the same time losing something of its frothy appearance. A bloody discoloration is usually to be noted, but the sputum is always less rusty than that of lobar pneumonia. The physical examination findings do not signify lobar pneumonia and they may be insignificant, but they usually suggest a catarrhal pneumonia, moist râles and crepitation being heard, especially at the bases. As the disease advances, the typical facial expression of bubonic plague changes to an apathetic or vacant one, a grave rather than a favorable sign. Delirium, active or quiet, is the rule in pulmonary plague. The temperature is high and irregular, and there may be a terminal drop just before death. Recovery is uncommon and, as previously stated, this variety of plague is the most fatal. Gotschlich has shown that pest bacilli, capable of killing guinea pigs, can be recovered from the sputum as late as forty-eight days after the temperature returns to normal. (Sandwith, Medical Diseases of Egypt, 1905, p.

169.) This is probably an extreme period, however, three weeks ordinarily sufficing to rid the sputum of living pest bacilli. This fact has important bearing upon the treatment of convalescents from pneumonic plague.

Treatment. The one melancholy phase of the entire subject of pest is the tardy progress that we have made in its successful treatment. It is true that the causative organism of plague has been definitely known for but ten years, and that much information relating to the specific cause and prevention of the disease has been accumulated during this time. It is also true, however, that these ten years have witnessed a destructive pandemic of plague, especially throughout the Eastern hemisphere, of the most unusual proportions. The record of the cost of plague during the decade, expressed in human lives and extending into millions, is the most eloquent possible appeal for an effective curative treatment, and as yet we are only able to respond with conditional, but hopeful, promises of relief. Prophylactic treatment, for the individual and the community, has already been considered. While statistical tables may be marshalled to show the favorable results of protective inoculation against plague, these tables usually apply to restricted and limited districts, and they do not indicate the truth, that the general application of the method is usually impracticable on account of the difficulties in securing acquiescence on the part of the population, and sufficient "plague-vaccine" and vaccinators. The same obstacles to the general use of a curative serum would doubtless obtain among ignorant or superstitious people, in some degree, if we possessed an effective and proven serum.

As a matter of fact, however, the *status præsens* of serum therapy in plague cannot be looked upon as more than promising. The use of antiplague serum is based upon the theory of neutralization of plague toxins in the human body, by the antidotal principles present in the serum of animals inoculated with plague bacilli and rendered immune by repeated inoculations. From analogy and a certain amount of experimentation the basic theory seems to be tenable, and the treatment, accordingly, rational. Of a similar kind, are the efforts and propositions to inject or adminis-

ter to plague patients drugs destructive to bacillus pestis, with a view to destroying the bacilli or toxins in the circulating blood, or at least to prevent their multiplication. There seems to be less reason to expect success along these lines, however, than from the administration of antipest serum. Yersin, Calmette, Roux, Borrel, Lustig, Terni, Bondi, Kitasato, and others have all elaborated sera, usually from the immunized horse, and these several preparations seem to vary greatly in strength and efficiency. A similar variation in the virulence and fatality of the disease is observed in studying different epidemics of plague, or the different periods of the same epidemic. Simpson points out that "the value of a serum for the specific or curative treatment of plague cannot be determined by one or two series of test experiments but that it needs many series of trials under varying circumstances before anything like an accurate estimate of its efficiency or antidotal power can be made." "The serum which shall possess evident and indisputable specific or antidotal powers against plague during an epidemic has still to be discovered."

He arrives at this conclusion after an analysis of the reports of the use of a number of preparations of antipest serum, in a number of epidemics of varying severity, in different parts of the world. These reports show a case mortality of from seven percent to eighty-one percent, the former figure being far below that reported from any other method of treatment and the latter being much higher than that of many reported epidemics where serum was not used. The matters of standardization and dosage of serum are entirely unsettled as yet. No lasting bad effects from the injection of antipest serum have been recorded. In Manila, in 1900, Yersin's antipest serum was found to be useless, while a small amount of the Japanese serum, sufficient for trial in three cases only, gave a mortality of $33\frac{1}{3}$ percent. Whether or not the Paris-made serum used unsuccessfully in Hong-kong and elsewhere had deteriorated from age or transporting is a question worthy of investigation.

In 1901 in Hong-kong the administration of carbolic acid to plague cases, with a view to destroying the bacilli and

toxins, or of preventing their multiplication, was tried in 204 cases, 80 grains (5. + grams) per day being administered. The mortality under this treatment was 76.5 percent. Again, in 1903, the carbolic acid treatment was proposed and administered in a series of 143 cases, and with a mortality of but 36.4 percent. In the later series Dr. J. C. Thomson administered the carbolic acid in a mixture of orange syrup and chloroform water in doses of 12 grains (0.8 grams) every two hours. In one case, 2500 grains of carbolic acid was administered to a patient before pest bacilli entirely disappeared from the blood. Poisoning with the drug was not noted and only exceptionally did carboluria occur. When it appeared, a dose or two of carbolic acid was omitted and the urine became clear, the treatment then being renewed. (Report on Plague Cases Treated in the Kennedy Town Hospital, Hong-kong, J. C. Thomson, M. D., 1903.) A control series of 139 cases untreated by carbolic acid, but observed early in the same epidemic, was observed by Dr. Thomson and a mortality of 85.7 percent was recorded for this series. An unusual number of mild cases included in this series, treated by the "antiseptic method," and the declining virulency of the disease, observed during the last half of the epidemic, unfortunately lessens the force of these statistics. It is to be hoped that further observation may prove this method to be one of real value in the treatment of plague.

Outside of the serum treatment and the "antiseptic" treatment of plague, we have to fall back upon symptomatic and supportant treatment by drugs and nursing. Considering the latter, and perhaps the more important matter, first, we find that the nursing of plague cases is a difficult and dangerous occupation, requiring intelligence and fearlessness. An appreciation of the dangers incurred, of the responsibility of enforcing isolation, and of the importance of a painstaking attention to the details of prevention already set forth, are necessary on the part of the nurse. The patient must be confined to bed, carefully dieted, his various excreta must be rendered harmless by disinfection, he must be restrained in the event of delirium and his strength must be con-

served in every possible manner to prevent sudden collapse from exhaustion.

The nurse must likewise have an understanding of antiseptic surgical dressings, fomentations, and the emergency treatment of hemorrhage. While the police duty of maintaining isolation should not be exacted of the nurse, he should be alert to prevent violations of the quarantine by others. The surroundings should be the most hygienic possible. Sunlight, abundant fresh air, and ventilation are of the utmost importance. For these reasons treatment in tents, when possible, has much to recommend it. A definite value, at least for disinfecting purposes, may be ascribed to the direct sun rays in tent-treated cases.

Cold sponging should be given for pyrexia. Ice, in the form of pellets to assuage thirst, and applied to the head in ice caps for headache and delirium, is a great boon which the patient in the tropics is sometimes denied.

Throughout the acute stage of plague the diet should be limited to liquids, or soft foods requiring little or no digestion. Peptonized milk, egg albumen, barley water and junket, combined with stimulants, according to the degree of toxemia present, are appropriate articles of diet. Food should be given in moderate amounts and at intervals of three hours, rather than at long intervals and in greater amounts. Often the appetite is ravenous, or it may be practically lost. Thirst is almost always a distressing symptom and if vomiting is a prominent feature the administration of nourishment and the quenching of thirst may be difficult. Whiskey, or brandy, properly diluted, sherry, or champagne in certain cases with intolerant stomachs, are appropriate stimulants and should be given according to the indications in the particular case.

The drug treatment is usually inaugurated by a mercurial purge of 5 grains (324 mg.) of blue mass or calomel, followed in six hours by a saline aperient. In every case an armed expectancy with regard to sudden cardiac failure must be maintained and drugs to avert or combat threatened collapse, such as ammonia, camphor, digitalis or strophanthus may be given for effect. Nitro-

glycerine or amyl nitrite may be used in emergency and strychnine, in doses from $\frac{1}{40}$ grain to $\frac{1}{20}$ grain every three hours to six hours, may be used with advantage. Opium or its derivatives will probably be needed to control pain. Morphine by needle, in $\frac{1}{4}$ grain doses, will serve us best. It may also be required to produce sleep and the bromides and other hypnotics may also be required in cases of violent delirium, but morphine in doses from $\frac{1}{6}$ grain to $\frac{1}{2}$ grain, by needle, will be found to be the most useful and least dangerous. Depressant antipyretic drugs should not be given and in the entire matter of drug giving the indications should be carefully studied and the effects closely watched. Diarrhea may be combated with intestinal antiseptics, antifermentatives, and if necessary with opium. If the acute stage of the disease be survived, the supportant side of the treatment should be carefully looked to. Iron is, perhaps, the most valuable drug in long-continued suppuration and during convalescence. Other tonics, bitter and constructive, may be useful, and appropriate feeding with a view to tissue building should receive special attention. Intercurrent diseases developing during convalescence, or present before the plague infection is incurred, as, for example, malarial disease, dengue, dysentery, or syphilis, should receive appropriate treatment.

The *surgical treatment* of plague includes the treatment of buboes and of the so-called "carbuncles." It may also include the checking of hemorrhage in extensive suppurative conditions. Whether or not the bubo should be extirpated has long been a disputed question of treatment. The weight of opinion seems to be favorable to noninterference prior to suppuration, upon which occurrence incision should be performed. In support of this teaching is the fact that other glands beyond the primary first-order bubo are almost invariably invaded before the initial bubo is sufficiently developed to suggest extirpation. This being the case, removal of the initial bubonic gland would not remove the infection, while complete removal of the involved chain of glands would seldom be possible. Exceptionally, in a small, well-localized group of glands, extirpation might be good practice. Ice bags applied to the inflamed and tender bubo may mitigate

the pain but hot antiseptic poultices or hot anodyne applications probably hasten suppuration and the time for incision. Free incision into the bubo, with drainage by gauze wicks or otherwise, should be made when evidences of pus are present. Antiseptic dressings should then be applied and frequently changed so long as suppuration persists.

Treatment of the plague "carbuncle," so-called, consists in the application of antiseptic, absorbent dressings, moist by preference, and the removal of the slough. In exceptional cases the infected skin area and the tissues beneath may be excised. If this be deemed available the electro-cautery knife might be used advantageously, the cautery knife sealing the lymph vessels and blood vessels as it divides them.

The treatment for glandular, circulatory and respiratory plague does not differ in any essential points. Pulmonary symptoms are not apt to require special medication and external applications to the chest cannot possibly alter the course of the disease.

LABORATORY DETECTION OF BACILLUS PESTIS.

MORPHOLOGY, CULTIVATION, STAINING, VITALITY AND VIRULENCE.

Bacillus pestis is a short rod with rounded ends and measures from 0.8 to 2 microns long and from 0.4 to 0.8 of a micron thick.

A capsule or pseudo-capsule can usually be made out. The bacillus is nonmotile, aërobic and does not form spores and one or two observers claim to have demonstrated a terminal flagellum.

It grows on blood serum, in from twenty-four to forty-eight hours appearing as a moist, abundant, yellowish growth and without liquefying the medium. On agar, or gelatine agar, this growth is grayish-white in color. On agar plate cultures, circular individual colonies with moist surfaces appear. At first these colonies are transparent but grow opaque towards the centres, with age. In bouillon cultures the fluid remains clear and a granular deposit forms on the sides and the bottom of the tube. The most favorable temperature for growth is one less than the body temperature, from 25° C. to 30° C.

When stained the bacillus may resemble a diplococcus, on account of its bipolar staining properties, especially when overstained with carbol fuchsin. Methylene blue, fuchsin and gentian violet, in aqueous solutions, all stain the organism fairly well, while Gram's method decolorizes it. The bipolar staining may be present in nearly all of the bacilli in a given preparation or in but a few of them. Besides the typical bacillus we often encounter varied forms of the organism, some elongated and slender, others globular or irregular, and the involution forms of the bacillus are extremely

Fig. 27.—Stalactite growth of bacillus pestis in bouillon. (Reproduced, by kind permission, from Simpson's Treatise on Plague, 1905.)

varied. Cultures should be made if doubt arises as to identity. Haffkine discovered that if a few drops of oil, either olive or linseed, be added to a flask of bouillon culture a peculiar stalactite growth of bacilli occurs. The oil should be added to the bouillon and the whole sterilized before inoculation. After inoculation the flask must be kept perfectly still, as vibration will prevent the stalactite formation.

After about three days flake-like colonies of bacilli attach them-

selves to the under sides of the floating oil globules and grow downward in stalactite-like form. This growth is very characteristic.

The plague bacilli is resistant to great cold, cultures remaining alive at freezing temperature and even at —20° C. Heat, on the other hand, either dry or moist, destroys the vitality of the bacillus at comparatively low temperature, almost any temperature above 50° C. being fatal if sufficiently prolonged. Different cultures seem to possess different resisting powers, but 80° C., sustained for fifteen minutes, is probably fatal to all of the bacilli and 100° C. of moist heat (boiling temperature of water), is at once fatal to all organisms; dry heat at 100° C. requiring an exposure of twenty minutes or more. For unexplained reasons the virulence of plague bacilli may be intensified or weakened by culture. Drying at high temperatures (the body heat or above), destroys the bacilli, while alternate drying and moisture both destroys and desiccates them. Direct sun rays, especially the rays of a tropic sun, lessen the vitality and virulence of the organisms.

Smears of the tissues, or scrapings of the buboes or involved lymphatic glands, or films of blood withdrawn from the circulation with a hypodermic syringe, or of serous fluid from peribubonic tissues obtained in the same manner, may be fixed and stained immediately or cultures may be made. Urine may be centrifugated and the precipitate may be examined or cultured for plague bacilli.

A number of valuable lives have been lost through experimentation in the laboratory with plague bacilli cultures, and by inhalation infection at the bed-side, on the part of medical attendants and nurses of patients suffering with plague, especially of the pneumonic (respiratory) variety. The utmost care should be exercised in working with the organism. For such persons as find it necessary to constantly work with cultures of plague bacilli, protective inoculation, according to the method of Haffkine or of Yersin, is advised. On account of the dangerous character of the organism, it is suggested that fixation with the alcohol flame be immediately followed by immersion of the fixed cover-glass film in a solution of bichloride of mercury, 1 : 1000, to assure destruction

of the organism, the brief exposure of the smear to the alcohol flame, in passing it through for fixation, being inadequate to kill the organism.

The procedure is as follows: Prepare the smear, dry it and fix by passing quickly through a Bunsen or an alcohol flame three times, or by immersion in equal parts of absolute alcohol and ether for half an hour. After fixation subject the film to 1:1000 bichloride of mercury solution, to assure the death of the bacilli. Next dry and stain by exposing the smear or film to a carbol fuchsin solution, or to Löffler's methyl blue solution, for three or four minutes. This method is most apt to produce the bipolar staining which is rather characteristic, especially if the specimen be first subjected to Gram's method. Wash thoroughly in water. The film may be mounted in water for a preliminary examination or Canada balsam may be used and a permanent mount made.

CHAPTER IV.

DENGUE.

Synonyms. Breakbone Fever; Dandy Fever.

Definition. Dengue is an acute infectious febrile disease, of undetermined causation, prevalent in epidemic form in many tropical and subtropical countries of both the Eastern and Western hemispheres. It is characterized by fever, frequently of two paroxysms with an intermission, rheumatoid pains in the joints and tendons and a severe degree of muscular soreness, and is accompanied by a polyform skin eruption, terminal as to time of occurrence, and frequently by an initial erythema. It is a self-limited disease and is practically nonfatal.

Facts of Geography and History. The geographical distribution of dengue is extremely far-reaching and the disease is known to medical observers and writers of all countries whose territories or colonies approach the tropical parallels.

Since the United States has acquired tropical possessions in both hemispheres, and has undertaken the construction of the ship canal across the Isthmus of Panama, this disease has greatly increased in importance to Americans.

Dengue is found in the southern parts of the United States proper, in Cuba, Porto Rico, Central America, Hawaii and the Philippines, and it therefore decidedly concerns American medical men. Among the countries of the globe where dengue flourishes, not already mentioned, are China, Java, Borneo, India, Asia Minor, Africa, and South America.

While varying somewhat as to type, dengue is essentially the same disease, in whatever quarter of the globe it is encountered. Of all known diseases it is probably the most truly and consistently epidemic in its occurrence. Whether or not it ever occurs sporadically cannot yet be definitely stated. Epidemics of very great magnitude have visited so many parts of the tropical world that

reference to individual epidemics is scarcely necessary. One of recent date that occurred within our own national boundaries was that which visited Galveston, Texas, in 1897, at which time 20,000 cases occurred within a few months. Should a more dangerous epidemic disease than dengue attain such proportions as these, the degree of medical interest and alarm would be very great. The total amount of suffering and disability, however temporary, which attends an epidemic of dengue is sufficiently great and distressing to warrant a closer study of the disease.

It is often stated that the sea coast regions are most frequently visited by epidemic dengue, and that a pronounced elevation above the sea is a circumstance unfavorable for the spread of the disease. So many instances of epidemics occurring in the interior, and at altitudes of several thousand feet above the sea level, are on record, however, that these views cannot be insisted upon. On the other hand, high temperature, or summer heat at least, seems to be a constant if not an essential condition for the spread of dengue.

Etiology and Prophylaxis. As stated in the definition, the cause of dengue is as yet unknown. Within the last few years one or two observers have announced the discovery of certain hemamebas in the blood of persons suffering from dengue, but these claims are as yet unconfirmed.

After a study of 500 cases of dengue in Beyrout, Syria, Graham announced that small, nonpigmented, intra-corpuscular blood parasites, resembling the hyaline stages of malaria hemamebas, but smaller, had been observed in one hundred cases. (N. Y. Medical Record, Feb. 8, 1902.) He also claims to have found this parasite in the body of a Culex mosquito, where it developed more rapidly than the malaria parasite, spores appearing in the insect's salivary glands within forty-eight hours. It is also reported that inoculations of a preparation of the mosquito's spore-containing salivary glands produced dengue in a human individual.

Another observer sent from the Philippine Islands to Washington a set of beautifully executed drawings of what he believed to be the dengue organism. By experts these drawings were stated

to resemble artefacts and the observations, doubtless made in good faith, were not accepted as convincing evidences of the truth of an attractive theory. Numerous observers elsewhere have repeatedly failed to find bodies resembling blood parasites in the blood, and the slight degree of blood destruction in dengue does not suggest an intra-corpuscular parasite. The hemoglobin index was also found by Sutton, Assistant Surgeon, United States Navy, to be above rather than below the normal (Journal American Medical Association, Dec. 17, 1904) in cases observed in Panama. Immediately following the first announcement by Graham of the presence of an hemameba in dengue I had the opportunity of examining the blood in a number of cases in the Philippine Islands. Although familiar with the appearance of hemamebas in malaria, from two years' constant study of them in Cuba and in the United States, I was unable to discover similar bodies in the blood of numerous dengue patients. Moreover, leucocytosis was the rule in all of the dengue cases in which I made blood examinations, in contrast to the condition that is observed in the blood of malaria patients. Sutton and Carpenter, however, in the Isthmus of Panama, found that there was a decrease in the number of leucocytes and a relative preponderance of the small mononuclears, in the cases studied by them.

Without desiring to discredit the hemameba theory of causation in dengue, I am impressed with certain points of dissimilarity to malaria which suggest that the theory is not well founded. These are the brief period of incubation; the self-limited character of the disease; the rapidity with which it spreads, and its resemblance to certain exanthematous diseases and to influenza, the latter, at least, known to be of bacterial origin. I should, however, be glad to relinquish views based upon impressions and negative evidence if the contentions of Graham be adequately confirmed.

McLaughlin found micrococci in the blood of dengue patients in Texas but a causative relationship to the disease can hardly be insisted upon, as yet, for any organism thus far described, upon the evidence submitted.

The *prophylaxis* of dengue need not engage our attention long nor seriously, as it must be admitted that no effective measures of prophylaxis are known. With the discovery of the cause of dengue rational prevention may suggest itself. At present it is quite as impracticable for the newcomer in the tropics to avoid dengue, if it chances to be prevalent in the community, as it is for one to avoid epidemic influenza in a temperate climate. In both cases he may escape, but not through any known human device. The personal immunity conferred by an attack of dengue is an extremely variable one. Doubtless there is a temporary protection in most cases but it can neither be measured nor estimated, and many well-authenticated cases of second attacks within a year, or even a few months, are reported. In the Philippines I observed two frank attacks, in an individual of my own household, within a year. Dengue is admittedly infectious, and highly so, but whether or not it is contagious is an unsettled question as yet. There seems to be a special susceptibility upon the part of newcomers, recently arrived from cold or temperate countries, but the natives are by no means immune. From fifty to seventy-five percent. of the population may be stricken with the disease within a month. In fact, epidemics do not commonly extend beyond two months, the supply of susceptible subjects usually being exhausted within this time. It should not be imagined, however, that all outbreaks of the disease assume such proportions. A single section of a town or other community may be invaded by the disease, or an epidemic may suddenly come to an end when it appears to be but half spent.

The incubation period is doubtless a brief one and is variously stated to be from one to five days. The average is less than three days and some cases develop within twenty-four hours after exposure.

Pathology. As dengue is a disease in which the mortality is practically nil, opportunities for the study of its pathologic anatomy are rare. Such few studies as have been made, postmortem, have not disclosed any constant pathologic lesions that may be considered in any sense characteristic. While complications

are uncommon there seems to be no good reason why dengue may not occur coincidentally with other diseases. In fact I have seen it occur, during epidemics, in both dysenteric and malarial patients detained in the hospital.

Diagnosis. Remembering the fact that dengue is rather strictly a tropic or subtropic disease, one will not frequently be called upon to diagnose between it and *influenza*, one of the diseases which it most closely resembles clinically. Should epidemics of dengue and influenza occur at the same time and place, it may be necessary to discriminate between them. In neither disease is there any reliable blood or serum test, but in influenza the specific bacillus is demonstrable in the bronchial and nasal secretions, by staining and microscopic examinations. Catarrhal symptoms are usually prominent in influenza and are usually absent in dengue. There is no skin eruption in influenza. The pains of influenza are less definite and less severe than in dengue.

The likeness of dengue to *measles* is not very striking. The coryza and long incubation period of measles are absent in dengue, and the arthritic pains of dengue are not present in measles. The skin eruption of measles is regular and definite in character, while that of dengue is polyform and terminal as to time.

The eruption of *scarlet fever* is early and that of dengue is late. Angina is present in scarlatina but not in dengue.

Yellow fever and dengue, although both epidemic tropic diseases with alterations of the color of the skin, should not be confused. The icteric discoloration of the skin in yellow fever does not closely resemble the early erythema nor the late eruption of dengue. The characteristic slow pulse (relative to temperature) noted in yellow fever, is not ordinarily observed in cases of dengue.

Albuminuria is common in yellow fever and rare in dengue. Yellow fever epidemics are amenable to control; those of dengue are not. Deaths are common in yellow fever epidemics and practically unknown in dengue. Joint pains and inflammations are unusual in yellow fever but constant in dengue.

Rheumatic fever, or articular rheumatism, resembles dengue as to the character of its pains but it is not epidemic, is far less

self-limited and is noneruptive (except in occasional cases of peliosis rheumatica). Joint swelling is greater and the prognosis is decidedly graver. Endocarditis does not occur in dengue.

Dengue and *malarial disease* resemble each other chiefly in the fact that both are febrile. Blood examination for malaria parasites is diagnostic, repeated negative findings excluding malarial disease.

Symptoms. Dengue has been described as "an arthritic fever with a cutaneous eruption." This is not an inappropriate description and epitomizes the most striking characteristics of the malady. As I have pointed out, the disease wherever found is essentially the same, whatever the variations of type may be. There has been much discussion as to whether or not the skin eruption is ever absent in dengue. By some observers it is looked upon as a disease in the class of true exanthemata, while others do not consider it an eruptive disease, looking upon the eruption as something inconstant and almost incidental, the claim sometimes being made that entire epidemics occur without eruptive cases. I should be inclined to doubt the diagnosis under such circumstances. Certainly it has been my experience that cases of dengue rarely, if ever, occur without eruptive symptoms.

We are all familiar with the varying intensities and vividness of eruptions in the ordinary exanthemata of cool climates, and it is not hard to understand how such an eruption as that of dengue, occurring at the close of the fever, may frequently be overlooked. Particularly is this true of dark skinned races and individuals, Negroes, Malays, Mongolians, and brunette Caucasians, especially those with coats of tropical tan.

The onset of the disease is rather sudden. There is usually a prodromal period of several hours, marked by lassitude and indisposition, but occasionally one is attacked sharply and suddenly, when in excellent health and spirits. Or he may retire in health and awake with the joint pains and fever well established. The tongue is not particularly furred nor are nausea and vomiting usually present at the onset. Later, however, particularly in the second stage, the digestive functions are deranged, and vomit-

ing, constipation or diarrhea may develop. During the first two days fever is continuous and often high, attaining at times 104°, or 105° F. The pulse is in correspondence with the temperature and is hard and bounding. One or two chills may occur. During this period the joint pains and backache are extremely severe. Some special group of joints usually gives evidence of decided inflammation, as for instance the fingers and wrist of one hand, or the knee and ankle joints of the same extremity. This joint, or group of joints, usually remains inflamed during the course of the disease, although other joints may become stiff and painful. The aching in the back is of such degree as to earn the description "bone-breaking," while the headache may be extremely severe, the eyeballs aching and showing injection. In a sharp attack which I suffered in Manila, in 1902, the headache was more endurable than the joint and muscle pains, which were excruciating. Locomotion or movement is impossible and the prostration is extreme. There is no true eruption during this first stage of dengue, but the high fever may produce great congestion of the face or erythema, and this may even be apparent in the buccal and pharyngeal mucous membranes.

This extremely distressing state of affairs is maintained for about forty-eight hours when a critical sweating occurs and the severity of all the symptoms abates, or the fever and accompanying morbid phenomena disappear, closing the acute first stage of the disease. The acute period may be protracted to seventy-two hours and the disease may pass by lysis into the milder second stage. In some cases the second stage is not observed. At the time of crisis there may be bleeding from the nose, or diarrhea.

A calmer period varying in length from twenty-four to seventy-two hours, the period of intermission or remission, usually follows the stormy first stage. During this time temperature and pulse may be normal and the patient comfortable enough to leave his bed or resume his duties, though rarely free from the joint pains or stiffness.

The second stage now ensues in which the joint and muscle pains, and the fever, may occur in a degree almost equal to the

severity of the first stage, but usually all the symptoms are decidedly milder, and at the end of twenty-four hours the eruption occurs, followed closely by a second crisis. In the second stage the temperature will usually range from 100° F. to 102° F.

The dengue eruption, usually described as resembling measles, is decidedly multiform and may resemble in the same individual measles, rötheln, and scarlatina. In color it varies from dusky red to rose and scarlet, and it may appear upon any part of the body, including the palms of the hands. It is especially liable to appear upon the flexor surfaces of arms, wrists and thighs, and may at times be almost universal. It may be macular, papular or diffuse and often occurs as eruptive islands, surrounded by clear, sound skin, or islands of sound skin may be left in an extensive field of diffuse rash. It may also be so slight, and of such brief duration, as to be overlooked. In some cases the rash is limited to dark red spots upon the palms of the hands, perceptibly raised but without the "shotty" sensation to the touch, which is peculiar to variola.

Itching or burning is noted in some cases and the rash usually disappears within three days, gradually fading away. Following the fading of the eruption, there is a desquamative shedding of the epidermis in rather fine scales, lasting a week or ten days. The convalescence, which sets in with the appearance of the rash and the cessation of the fever, is marked by lingering stiffness of the muscles, joint swellings, and pains indistinguishable from rheumatism, with consequent disability of the affected joints.

After disappearing, these pains may return and this condition may last for some weeks or even longer. Sciatica is one of the commoner sequellæ and is a distressing and rather intractable occurrence. While returning from Manila one of the passengers, a well-known medical officer, suffered continuously from sciatic soreness and knee-joint inflammation which, he informed me, had persisted after an attack of dengue suffered six months before.

During the acute stage of dengue swelling of the lymphatic glands of the groin, axilla or neck may occur, either with or without tenderness, and this condition often persists during the

convalescent stage. Sutton (loc. cit.) suggests that some of the causes of "idiopathic tropical buboes," so-called, met with in the Panama Canal Zone may depend upon initial attacks of dengue with adenitis. Other writers speak of persistent lymphatic swelling as one of the sequellæ of dengue.

The foregoing description is that of classic dengue as described by various writers and as observed by me in the Philippine

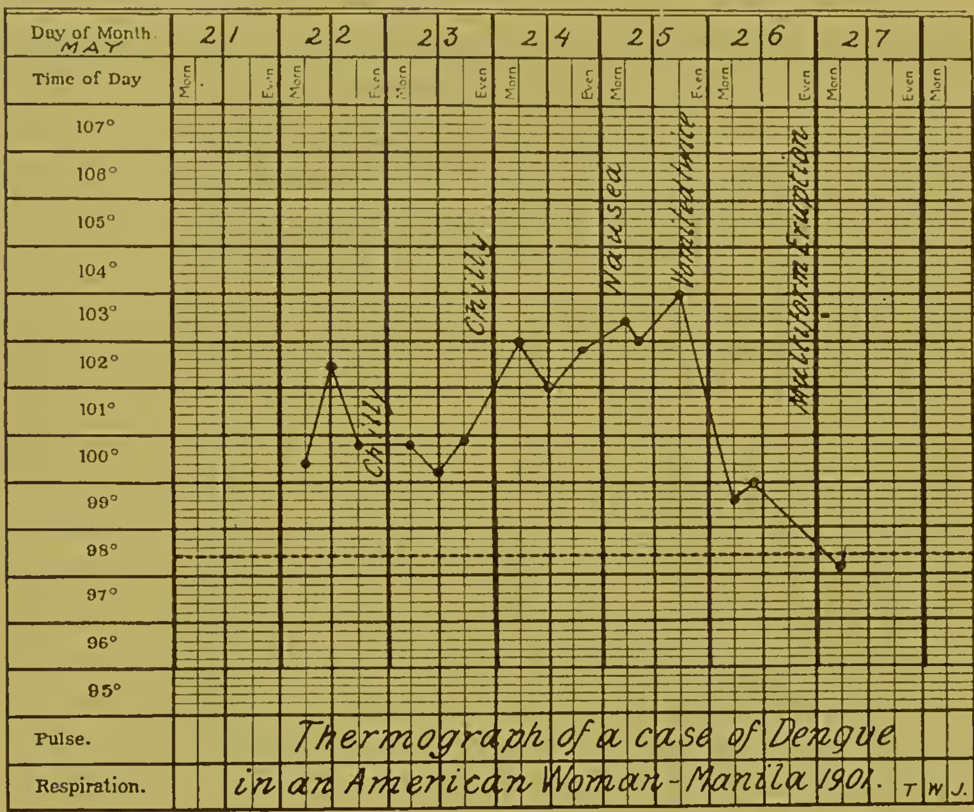


Fig. 28.

Islands. The above thermograph is that of an American woman, the wife of an army officer, whom I attended in Manila in 1901. Except for the incomplete character of the intermission on the second day, it is perfectly typical of dengue as I observed it in different places in the Philippine Islands. In a fairly large percentage of my cases the interruption in the fever which occurred between the first and second stages, was a remission rather than an intermission.

Having described the disease as it has appeared to me, it is only fair to state the observations of others who have noted marked deviations of dengue from the clinical course described. Thus in Cuba, in 1899, during a dengue epidemic at Quemados, which was at first looked upon as one of mild yellow fever, eruptions were noticed in but seven percent. of the cases reported by one surgeon, and the number of cases in which but a

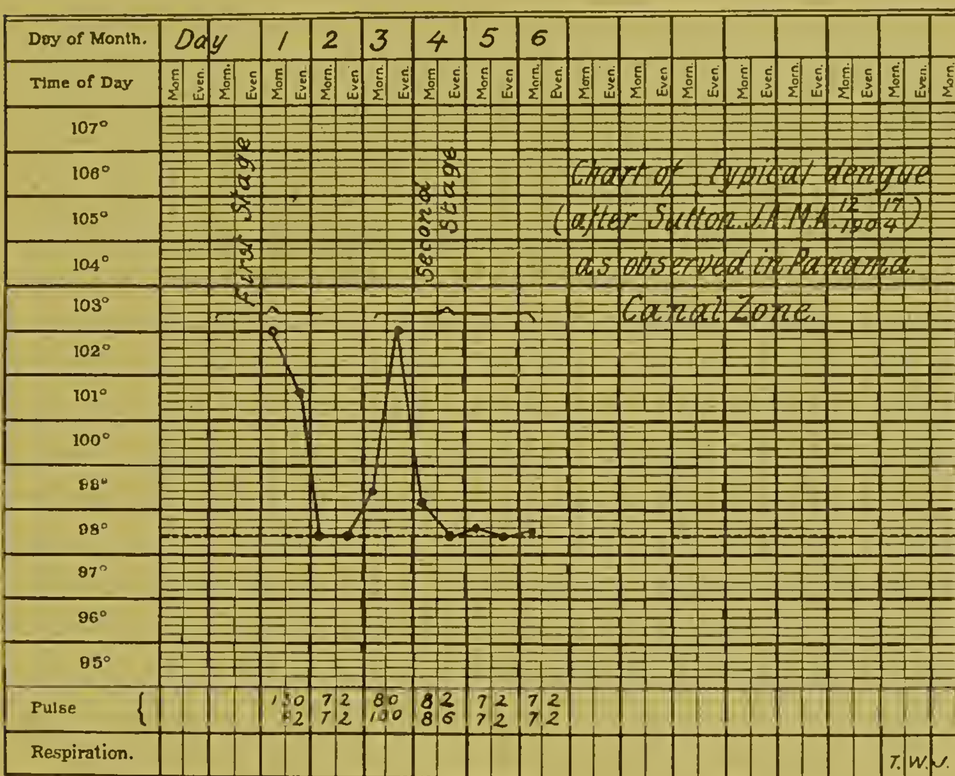


Fig. 29.

single paroxysm of fever was observed was large. In the Panama Canal Zone Sutton, United States Navy (loc. cit.), mentions the frequent absence of the initial erythema, often noting pallor in place of congestion. He also reports the frequent absence as well as the atypical character of the terminal eruption, and produces charts in which the secondary rise of temperature is absent.

In evidence of the fact that dengue produces considerable

disability in our new tropical possessions, I quote the following from the report of the Surgeon-General of the Army for the year ending June 30, 1902. "Dengue was almost absent from the United States, Cuba and Porto Rico, but quite prevalent in the Philippines, giving 31.67 cases per thousand of strength in the division." Again from the report for 1903-1904 we find that: "Dengue gave quite a large admission rate in the Pacific islands and China, where 2450 cases were admitted to sick reports, equivalent to a rate of 102.86 per thousand. No fatality was reported from this large number of cases. The rates of admission for troups serving in the United States and in Cuba and Porto Rico were 0.21 per thousand, and 2.56 per thousand respectively."

Treatment. Until such time as the causation of dengue is definitely determined, our treatment must needs be empiric and symptomatic. At present there is no specific indication to do more than to treat the distressing symptoms. Preventive treatment, at least so far as quarantine is concerned, is useless. In order to avoid an epidemic of dengue one must leave the vicinity. Perhaps I have not laid sufficient emphasis upon the fact that dengue is extremely infectious (perhaps contagious) and attacks all persons in its path, regardless of age, sex or color. At one station in the Philippines all the members of my household except myself, four persons, including two Filipino servants, were striken at once, all within twenty-four hours. At the same time a native "practicante" or doctor, of whom I made inquiry, assured me that scarcely a house in the town and vicinity was without a case of "calentura" at that time and took me into several households to verify his statements, which I did, finding the disease to be pure dengue. The natives, laity and "practicantes," seemed to recognize, doubtless from previous experience, that the malady was self-limited and without danger to life, and accepted the situation quietly. A stranger, or even a resident not in close touch with the natives of the community, probably would have been unaware of the epidemic.

The indications are to make the dengue patient as comfortable as possible. Quinine need not be considered, as it possesses no

virtues whatever in the treatment of dengue and is incapable of arresting or aborting an attack. Hyperpyrexia may demand treatment, by cold sponging preferably, or by drugs. Phenactin, 5 grains, or acetanlid, 5 grains, in combination with codein $\frac{1}{4}$ grain, may be used every two hours if necessary for high temperature. If they fail to affect the temperature markedly they will probably give some relief from the pains. I should prefer to depend upon opium derivatives, morphine or codein in small doses, for the relief of pains, if drugs are required. Aconite lessens blood pressure and thus relieves headache. Ice (not always to be had in the tropics), or heat, locally applied, gives considerable relief. The ice bag to an aching head or joint, or hot fomentations to joints and muscles are comforting, and frequently a hypodermic injection of $\frac{1}{4}$ grain of morphine is merciful. Cool drinks, pure water, lime juice, or lemonade, should be given freely. Salol and the salicylates for joint involvement seem to do good, particularly in the second stage and during convalescence. Free purgation is not known to affect the course of the disease in the least, but on general principles the bowels should be promptly unloaded at the onset of the disease and activity of the bowel and kidney functions should be maintained.

The itching may demand some emolient antipruritic lotion or unguent, but ordinarily does not require treatment.

For the sequellæ of dengue tonics, iron, and a change of climate constitute appropriate treatment.

CHAPTER V.

TROPICAL DYSENTERY.

In this consideration of the subject of dysentery I shall omit that variety commonly known as catarrhal dysentery, as it is by no means a distinctly tropical disease, and I shall confine myself to the two great varieties which are so prevalent in our insular possessions, viz.: amebic dysentery and bacillary dysentery, otherwise known as specific infectious dysentery.

It can no longer be doubted that this division of tropical dysentery into two great varieties is abundantly justified by facts, and the American writers upon tropical medicine, at least, generally concede that this division is accurate so far as our knowledge extends, without denying the possible existence of other varieties of dysentery as yet unstudied and unclassified.

In these days of great mutability of pathologic and etiologic matters, one must exercise great caution in announcing, as facts, views which have not been subjected to the severest tests.

The past seven years have added greatly to our positive knowledge in these two diseases and I shall try to confine myself to proven facts in discussing them.

Amebic dysentery and **specific infectious** or **bacillary dysentery,** are distinct diseases, due to distinct specific organisms, with distinct clinical and pathological manifestations. It is true that they sometimes occur in combination and in such cases the clinical and pathological manifestations are confused and obscured.

We will discuss them separately and in the order named.

AMEBIC DYSENTERY.

Synonyms. Amebic Enteritis; Intestinal Amebiasis.

Definition. Amebic dysentery is an inflammatory disease of the colon due to the entameba dysenteriæ, prevalent in tropic

countries and characterized by ulcerations of the intestinal mucosa, frequent evacuations of mucous and bloody stools, tenesmus, irregular fever, a tendency to chronicity, and the frequent formation of hepatic abscesses which contain amebas.

Facts of Geography and History. Amebic dysentery has been recognized as a definite form of tropical dysentery for some years, although, until quite recently, there has been considerable doubt in the minds of occasional observers as to the causative relation of amebas found in the stools of dysenteric patients, to the disease.

In 1859 Lambl, in Prague, announced the discovery of organisms resembling amebas in human feces. Lösch in 1875, in St. Petersburg, found them in the stools of a dysenteric patient and carefully described them, and later experimentally produced a similar disease in a dog, by the injection of amebas contained in human feces into the bowel of the animal. He also named the organism "ameba coli." Numerous European clinicians and scientists confirmed his observations and in 1890, Osler, in the United States, found the organisms in both stools and liver abscess pus from the same individual. American verification followed Osler's discovery as promptly as European confirmation succeeded Lösch's case and Stengel, Dock, Councilman, Lafleur and others built up a superstructure of proof which remains unshaken. Councilman and Lafleur published a notable work upon amebic dysentery, based upon their studies, which has been widely read and quoted.

The work of American army surgeons in the Philippines during the past five years, however, has done much to clear up the subject of intestinal amebas and their manifestations. Special credit in this connection is due to Strong, Musgrave, and Clegg for work in Manila and to Craig for his work in San Francisco. In the light of all this work it is difficult to understand why certain European writers upon tropical diseases still contend that intestinal amebiasis bears simply an incidental relation to dysentery.

Etiology and Prophylaxis. While the presence of amebas in dysenteric stools has been recognized for some time, amebas, apparently identical with, or at least very similar to those found in

dysenteric stools, have been found in normal stools and intestines. This gave rise to the view that the organism was a single one, benign at times, but capable of taking on pathogenic properties under certain circumstances. The researches of Strong and Musgrave in Manila seemed to indicate rather conclusively that "there are at least two distinct forms of amebas found in human stools." One of them, the ameba dysenteriæ, is the cause of amebic dysentery and is capable of producing dysentery and dysenteric lesions in man, and in domestic animals, viz., cats. The other, ameba coli, is apparently not harmful to either. These observers say, "We have repeatedly injected large numbers of these nondysenteric amebas (ameba coli) while motile in the stools, into the rectums of cats, but with no effect." Similar procedure with motile amebas from the stools of dysenteric patients, produced both dysenteric stools and lesions in these animals. These experiments were conducted on an extensive scale, covering a considerable period of time. The nondysenteric amebas were obtained from the intestines of persons not suffering from dysentery. The investigators set out to find the ameba coli in stools from a number of persons, administering Rochelle salts to them and then examining the stools for amebas. They found the harmless amebas in about four percent. of these cases, and in one of the cases under observation amebas were present constantly for several months, without dysentery or the history of past dysentery. The investigations of these gentlemen are too voluminous for quotation here. (Report of the Surgeon-General of the Army, 1900, pp. 269-271.)

These conclusions and similar ones announced by other observers, particularly by Schaudinn (Untersuchungen über die Fortpflanzung einiger Rhizopoden, 1903), were accepted by many writers and the division of entamebas into entameba coli (nonpathogenic) and entameba histolytica or dysenteriæ (pathogenic), with differentiations according to the size of the organisms, the pathogenic being described as being larger than the innocent one, appears in some very recent works. It is not impossible that some corrections will have to be made in this classification.

In the latest important print upon intestinal amebiasis which has reached me, "Amebas: Their Cultivation and Etiologic Significance" by Musgrave and Clegg, Manila, appear certain experiments and observations concerning the classification of intestinal amebas which seem to modify the foregoing views concerning the division of amebas into pathogenic and non-pathogenic varieties. These observers have continued the work of Strong and others in Manila over a period of several years and present their observations in a somewhat remarkable report (October, 1904) which impresses the reader with its thoroughness and with its conservative tenor. The causative relation of amebas to amebic dysentery is strongly insisted upon and supported by experiments, and they have succeeded in cultivating, by symbiosis with certain bacteria, amebas from many sources, which appeared to be innocent or pathogenic according to circumstances. Their work and that of others seems to point to the impossibility of securing satisfactory pure cultures, but it also shows the possibility of cultivating a single species of ameba with pure cultures of a single kind of bacteria. Photomicrographs of plate cultures, of various ages, are shown and a practical technique is described. The student is referred for details to this interesting report. A few of the conclusions reached will be quoted.

"Amebas when present in water, soil and other places outside of the animal body may almost certainly be secured in culture and by the methods described pure species in pure cultures of bacteria may be obtained." "Amebas may be cultivated from dysentery stools and ulcers in the human bowels." "Living bacteria or other micro-organisms seem to be necessary to the existence of the amebas under artificial condition." "Amebas have not as yet been grown in pure culture. Whenever they have been freed from other micro-organisms by various methods they have refused to multiply on any known medium." "The cultivation of pure species of amebas has offered strong evidence of the plurality of species of these protozoa and this plurality apparently extends to those which produce infection in man." "Evidence brought forth to show the harmlessness of amebas

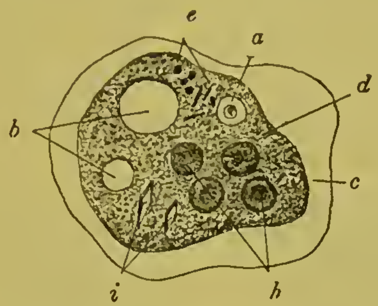
is not conclusive and certainly in the tropics the appearance of amebas in the stools should be sufficiently diagnostic for the institution of therapeutic measures, regardless of the nature of clinical symptoms."

They also state that: "It is certain that with our present knowledge the measurements of amebas from stools cannot be used for purposes of differentiation either as to species or as to pathogenicity," and they show that in cultures amebas vary greatly in morphology according to age, phase of life cycle, the density of media and other factors of environment. Amebas may be isolated and cultivated from soil, water, dust, dried hay, the surfaces of fruit and vegetables and from other sources. In the Philippine Islands they abound in surface waters and the city supply of Manila yields them readily. This is probably true of many other warm countries, particularly in the cities, where similar conditions exist. Their reactions to physical conditions and chemical agents have not been completely and positively determined but it is probable that drying, cold and light do not easily destroy them. Acid conditions and heat, if of sufficient degree, destroy, amebas while they resist alkaline conditions strongly. In view of their wide distribution in the tropics it is probable that but for the normal acidity of the gastric juice all intestines would be infested. Musgrave and Clegg maintain that the transient occurrence of amebas in normal intestines is rarer than is usually supposed. Various chemicals in solution have the power of inhibiting motility and of killing amebas. All the ordinary germicidal drugs, such as bichloride of mercury, potassium permanganate, hydrogen dioxide and phenol in weak solutions kill the organism upon contact and 32° F. and 110+° F. are fatal to the amebas of dysentery. Quinine solutions of 1:300, in water, destroy the organism after fifteen minutes' contact.

In San Francisco, Craig studied the pathological anatomy of a large number of cases of amebic dysentery and the morphology and staining properties of the organism. The motile amebas must be studied in the fresh specimen at the body temperature, but they may be fixed and stain beautifully, showing the organisms

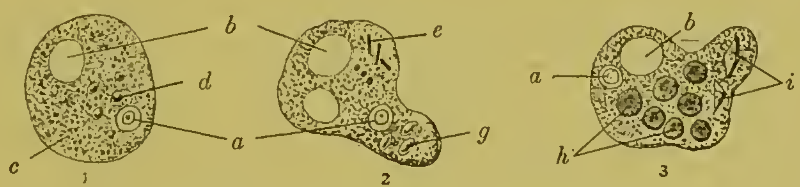
in various stages of ameboid movement. I have found this method of value in liver abscess cases, in searching for the organisms in the abscess contents.

The ameba can be found with a low power objective but



C. F. Craig, "International Clinics, 1904."
Fig. 30.—Diagram of entameba of dysentery.
a—Nucleus. *d*—Endosarc.
b—Vacuoles. *e*—Bacteria.
c—Ectosarc. *h*—Red blood cells.
i—Crystals.

considerable experience is necessary to recognize and differentiate it. "It is a round, oval or irregular protoplasmic body, varying in size from 5 to 35μ; motile or immotile (according to temperature); the motility ameboid in character when present, being



C. F. Craig, "International Clinics, 1904."
Fig. 31.—Illustrating bodies contained in entamebas of dysentery.

1 { *a*—Nucleus. *b*—Vacuole. *c*—Granular protoplasm.

2 { *a*—Nucleus. *b*—Vacuoles. *e*—Bacteria. *g*—Oval refractive bodies, probably spores.

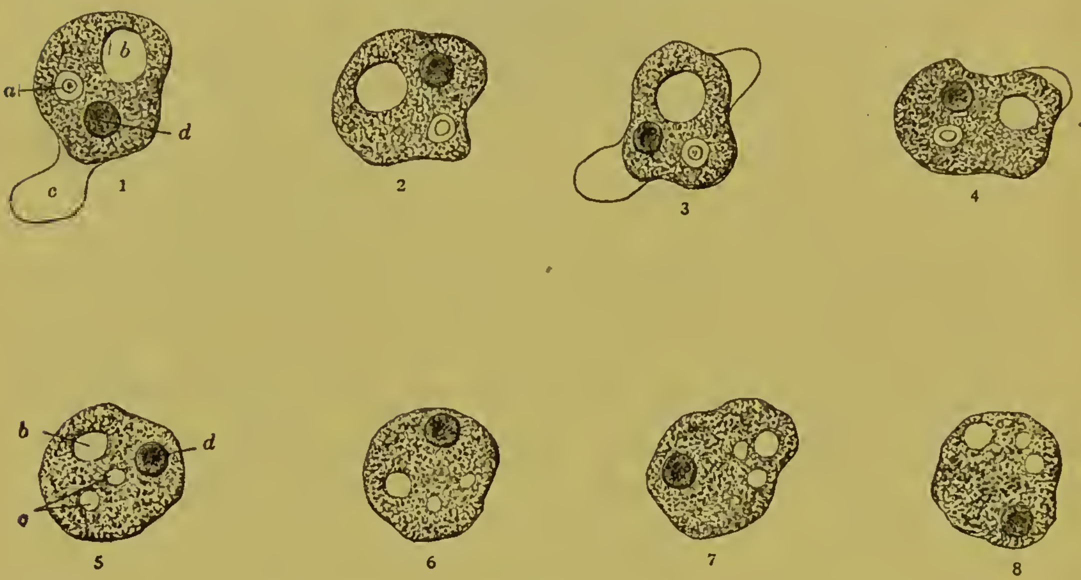
3 { *a*—Nucleus. *b*—Vacuole *h*—Red blood cells. *i*—Crystals.

generally moderate; pale or faint green in color; refractive, with a sharply cut border, and containing circular or oval lighter colored spaces, known as vacuoles.

"In some a darker colored nucleus can be distinguished, and in

the immotile organisms a darker colored central or excentric portion containing the vacuoles and comprising the greater part of the parasite, and known as the endoplasm, can be seen surrounded by a narrow or much smaller layer, lighter in color and clear, known as the ectoplasm." Medical News, N. Y., March 16, 1901. (Description from Craig.)

Concerning the methods of reproduction of the entameba dysenteriæ our knowledge is incomplete. Whether it occurs by fission



C. F. Craig, "International Clinics, 1904."

Fig. 32.—Upper line illustrates changes in shape of entameba without progressive motion. *a*—Nucleus. *b*—Vacuole. *c*—Pseudopodium composed of ectosarc. *d*—Red blood cell.

Lower line illustrates protoplasmic flowing motion, with changes in the position of the contents of the ameba without pseudopodia formation; changes being due to a current in the endosarc.

b—Vacuole. *c*—Very small Vacuoles. *d*—Red blood cell.

or sporulation, or both, is a question as yet undetermined. There is good evidence that fission occurs (it having been actually observed by a few men) but proof that the process is one of reproduction is entirely lacking. Recently Craig (International Clinics, Vol. 4, series 14, 1904) strongly supports the sporulation theory of reproduction, by argument and a series of colored drawings of the organism stained by a modification of Wright's method, whereby the finer structure of the ameba is well shown. These

plates depict the various stages of sporulation. This view has also been held by other writers and Schaudinn claimed to have demonstrated reproduction by sporulation. Craig (loc. cit.) states that he has confirmed Schaudinn's claim.

The best stains for entameba dysenteriæ are Löffler's methylene blue, thionin solution, Wright's stain and carbol-fuchsin.

The first and last named are easily used and generally available.

C. F. Craig, "International Clinics, 1904."

Fig. 33.—Illustrating changes in shape of entameba dysenteriæ during progressive motion. Changes in seven minutes' observation.

a—Nucleus. *b*—Vacuole. *c*—Pseudopodium, composed of estosarc. *d*—A red blood cell, free in the feces and later, engulfed in an ameba.

The procedure will be found in the section on laboratory detection. A property of entameba dysenteriæ which is of great value from the point of view of diagnosis is that of motility. This property is possessed by all living entamebas at the body temperature, becoming less and less pronounced as the temperature is lowered and disappearing long before the death point is reached. This

point is variously given by different observers but is probably about 70° F. Motility, when lost by cooling, may often be restored by gently warming the preparation. It will be observed that the motility is not only of the kind which causes the organism to progress by throwing out pseudopodia but that it causes the ameba to project and to withdraw them without progression and that undulations of the protoplasm, vibrations of the borders and a flowing of the protoplasm into and out of the pseudopodia, also occur. Staining of the living young amebas, by permitting weak solutions of certain dyes to run under cover-glass preparations, has also been successfully performed but has no great value. Neutral dyes only can be used in this manner and then in very weak solution, so that the differentiation of nuclei is not usually good. Motility is best studied in fresh unstained specimens at or near the body temperature.

The mode of infection is almost invariably through the ingestion of water or food products containing ameba. This being the case we have a valuable guide to *prophylaxis*.

Although amebas are found in many places their principal and original source is generally acknowledged to be water. So long as this is conceded and as uncertainty exists concerning the efficiency of other prophylactic measures, the only safe rule is to introduce into the alimentary canal no food or drink which has not been sterilized by heat. Natural immunity is not to be depended on though it is well known to exist in certain individuals. There is no way of determining who these individuals are or of measuring their immunity. Safe water is such as has been distilled, or boiled, and preserved from contamination during storage and dispensing. The same precautions that were recommended for the prevention of cholera are applicable to amebic dysentery and the same religious regularity and consistence in their observation are essential for success. That the control of these conditions by sanitary experts reduces the occurrence of amebic dysentery is conclusively proved by the statistics from Manila for July, 1904. These figures are quoted from Musgrave and Clegg (loc. cit.). During this month there were treated at the Civil Hospital and

by private physicians, 318 civil employes, drawn from 2500 civilians employed by the government. Of this number ninety had amebic dysentery. Of the 439 patients at the military hospital (First Reserve) drawn from 2742 troops, in the same month, there were nine cases of amebic dysentery. In other words more than three percent. of the civil employes suffered from the disease while but $\frac{3}{10}$ percent. of the soldiers were affected. This immunity on the part of the soldiers was directly due to enforced observance of sanitary provisions concerning the use of sterile water and sanitary food preparations, and in the case of the civilian employes, where the rate of incidence was ten times as great, the prevalence of amebic dysentery was explained by the lack of compulsion to use sterile water and food.

No comment could be more forcible than these quoted figures.

Pathology and Diagnosis. The primary and principal seat of the lesions in amebic dysentery is the colon, the lower foot or more of the small gut occasionally sharing in the destructive ulcerative process. The microscopic changes which take place begin in the mucosa, and redness and injection of this structure first occur. Then follow swelling and infiltration of the submucous structures, and necrotic destruction of epithelium, mucosa and submucosa down to the muscular and serous coats of the bowels. These ulcerations are originally oval in shape, becoming irregular in outline with gradually undermined edges. The ulcerated areas coalesce, often bridged over with sound mucous membrane until we have a system of submucous fistulæ uniting the original ulcerations. The necrotic epithelium and mucous membrane slough, and are passed from the bowel in the stools. The rectum and the sigmoid portion of the colon are, perhaps, the most frequent sites of this ulceration, although the entire colon is sometimes involved in cases of long standing. The cecum is frequently greatly involved. Amebas are found in the walls and floors of these ulcerations almost constantly. Perforation of the colon may take place, and if this occur in the cecum the condition may simulate a perforative appendicitis. I have seen the belly opened in a case of this character under the impression that the case was one of

appendicitis with perforation. An hepatic abscess was present in the same case.

In 100 autopsies for amebic dysentery upon American soldiers in Manila in 1900, by Strong and Musgrave, fourteen revealed lesions of the vermiform appendix and six of these were actual amebic lesions. In four of the six cases death was due to perforation of the cecum or colon by amebic ulcers and in every case the condition of amebic ulceration of the appendix was one of extension of the process from the cecum. The pathologic lesions of the gut are extremely typical and the naked eye appearance of the ulcerations is usually sufficiently characteristic to permit us to determine the variety of dysentery. In the Army Medical Museum at Washington, where there are preserved a large number of specimens of dysenteric intestines obtained during the epidemics of the Civil war, one is able to contrast the postmortem appearances of amebic dysentery of the tropics with the epidemic dysentery of the United States which prevailed in 1861 to 1865 and which was, in all probability, the disease to be described under the name of specific infectious dysentery. As has been stated the lesions are rarely found above the ileocecal valve and are most common in the rectum, cecum and sigmoid. Upon the outer coat of the intestine, which is gray in color, will be observed discolorations, dark brown or yellow, which do not correspond with the amebic ulcers upon the mucosa within. When gangrene occurs the usual gangrenous color and adhesions will be observed. Thickening of the intestinal coats is to be noted and upon the folds of mucosa extending into the lumen of the intestine small nodules, which later develop into amebic ulcers, appear early in the disease, but the preulcerative pathology of the intestine in amebic dysentery is not yet well determined.

It is believed by some that entameba dysenteriæ excretes a poisonous or solvent material, which destroys the mucosa and permits the organism to penetrate to the submucous coat and down to the muscularis which seems to bar its progress. Amebas are practically always to be found in the ulcers and in the submucous fistulæ. Evidence pointing to the occurrence of a toxemia due to

absorbed toxic products of the entameba dysenteriæ, is entirely wanting and such opinions are purely speculative. Although we know that such toxemias do occur in cholera and in bacillary dysentery, and that the systemic manifestations in these infections are most grave, we cannot extend the analogy to all infections of the intestine by animal parasites, as in the case of entameba dysenteriæ, at least in the present state of our knowledge. Nor can we expect any great good from antitoxic or serum treatment, either for immunizing or curative purposes.

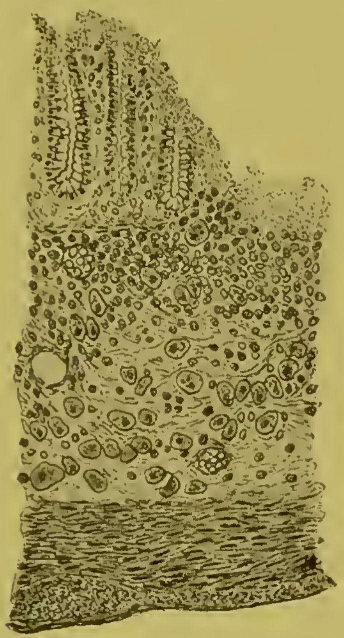


Fig. 34.—Section of colon wall at border of ulcer. Shows destruction of mucosa, thickening of submucosa and many amebas in submucosa. (From Tyson's Practice.)

The manifestations of entamebas dysenteriæ in the body outside of the intestine are practically confined to the liver. This organ is quite frequently the seat of abscesses, single or multiple, which contain the amebas and are directly due to their action upon the liver structure. They occur only in association with amebic dysentery and their cause is no longer a matter of doubt or speculation. Entamebas dysenteriæ reach the liver from the colon by way of the blood current, the direct route through the capillaries of the intestinal wall and the portal vein favoring their determination to this organ. They have even been observed within the capillaries, in microscopic sections of the intestinal wall. Other routes suggested are through the lymph channels and through the peritoneum. If migration occurs in any other way than via the portal vein it is probably through the peritoneum, as Councilman demonstrated amebas in peritonitic exudate and in an exudate upon the liver surface. Whether they cause necrosis of the liver structure mechanically, or by the solvent action of their products, is undetermined but the process is probably similar to the one in which they produce destruction of the colon

walls. The frequency of amebic abscess in dysentery has been most variously given. Where the percentage of *fatal* cases of dysentery showing amebic abscess is given the rate varies from thirty-five to seventy-five percent., but where the percentage of all cases, fatal and otherwise, is estimated it is much lower. In the United States army hospitals in Manila and San Francisco, where most of the invalided soldiers are brought, the rate of occurrence approximated five percent., or one case of liver abscess in every twenty cases of amebic dysentery.

The right lobe of the liver at its dome, or upon the under surface, is usually the first portion of the gland affected. These two points are in relation with the under surface of the diaphragm and the upper surface of the colon in its hepatic flexure, respectively. When other abscesses develop they are usually continuous or communicate with the original abscess cavity, and the matter of the number of cavities and their situation is not governed by any well-defined law. Abscesses are single or multiple and may even exceed ten in number, varying greatly in size from that of a hazel-nut to a cocoanut. Adhesion of the liver capsule to adjacent structures at or near the site of abscess is a common and favorable occurrence, often preventing the peritoneal extravasation of pus. The appearance of the abscess contents will depend upon the purity or admixture of the entamebas with pyogenic micrococci. About one-half of all cases are infected with pus organisms as well as amebas. This pus infection is always secondary, however.

If pus bacteria are absent the fluid contents of the abscess will be chocolate colored and the walls of the cavity will be ragged and shaggy, due to shreds of necrotic liver tissue, while in cases where pus infection has supervened the fluid will be yellowish-green and the walls will probably be smooth. In the smaller and more recent abscesses there will be no well-marked fibrous limitation of the cavity.

Rupture occurs frequently and may be into the abdominal cavity, pleural cavity, pericardium, lung, stomach or, indeed, into any adjacent organ, producing purulent peritonitis, empyema, pericarditis, abscess of the lung or other complications.

In twenty-four cases of liver abscess reported by Craig at San Francisco, in soldiers returned from the Philippines, there were seven cases of rupture, of which five were into the pleura and two into the pericardium. (P. 292, International Clinics, vol. 4, series 14.)

The diagnosis of amebic dysentery must rest upon the microscopic findings of entamebas in the stools, in conjunction with the clinical symptoms of dysentery. Without recourse to the microscope amebic dysentery may readily be confused with a number of diseases and conditions and, indeed, it will rarely be possible to positively diagnose amebic dysentery antemortem except in the presence of liver abscess. Postmortem it may be recognized by its typical lesions. Among the diseases and infections which must be differentiated are catarrhal dysentery, specific infectious dysentery, intestinal tuberculosis, typhoid fever, chronic gastro-enteritis, the intestinal manifestations of malarial disease (see chapter on Malarial Disease), and hook-worm disease. The essentially chronic character of amebic dysentery, with the tendency to relapse, is characteristic but not peculiar to the disease. From *tubercular ulceration* it may usually be differentiated by the history, the character of the stools and by the presence of tubercle bacilli and glandular involvement in tuberculosis. From *typhoid fever* it may be differentiated by the history and temperature curve and the Widal agglutination test. From *specific infectious dysentery* it may be differentiated by the fact that it is less acute of onset and less epidemic, and by the agglutination test for the Shiga bacillus. The absence of ova and *ankylostoma* from the stools in amebic dysentery (except in cases of infection with both amebas and hook-worms, which condition of double infection is not uncommon in the tropics) serves to differentiate it from ankylostomiasis. In the end, however, we are brought back to the microscope.

Without its use we cannot exclude *malarial disease*, nor can we discover the entameba nor make the serum tests for typhoid fever or specific infectious dysentery.

Once more let us remember that double infections, such as

malarial disease and amebic dysentery, and ankylostomiasis and amebic dysentery, are not unusual in the tropics. From *syphilitic* or *cancerous disease* of the rectum we must differentiate by the history, by inspection and by the presence of amebas in the stools. A single microscopic examination of the dysenteric stool with a negative finding should never justify a negative diagnosis if amebic dysentery is suspected. Painstaking and repeated searches should be made and occasionally a saline cathartic must be administered to secure specimens containing amebas.

The details of technique will be found under the heading of laboratory detection.

Symptoms and Treatment. Amebic dysentery is much less acute in its onset and progress than specific infectious dysentery. It usually begins as a moderate diarrhea, the stools at first being mucous in character, gradually becoming bloody and liquid and containing pus and necrotic tissue. In exceptional cases, however, the onset and course of the disease is quite rapid.

Gastric symptoms are often absent and pain is a far less prominent symptom than in the infectious variety of dysentery. Tenesmus is not marked and the stools do not frequently exceed fifteen or twenty per day. Fever is often absent, or, if present, is of a low, irregular type. The temperature may be subnormal throughout the disease but is usually irregularly febrile.

The healing process may occur at the same time that extension of ulceration is going on, and there is a decided tendency towards chronicity. I have personal knowledge of cases that have extended over four years, with intermissions of apparent good health. Nevertheless, the disease is attended with a considerable mortality rate and many cases die of intercurrent disease due to lowered vitality, and such complications as perforation of the bowel with peritonitis, liver abscess with perforation into the pleural cavity, with empyema, and from secondary anemia.

Many others suffer from disability and become chronic invalids.

Tenderness over the cecal and sigmoid regions, and moderate pain in the same regions, are usually present, particularly when at stool. Vomiting and nausea are not commonly present but

may occur during bowel movements or while enemata are being administered. The appetite is occasionally quite good and the craving for forbidden foods is often distressing. Gastric and even intestinal digestion is occasionally fairly well performed, even while dysenteric stools from the colon are being voided. The fever is rarely of sufficient severity to require treatment except when hepatic abscess occurs. Prostration, anemia, asthenia and emaciation are progressive in unfavorable cases, the patients occasionally resembling living skeletons before death ensues.

When liver abscess develops there are added the constitutional symptoms of suppuration, particularly if secondary pus infection of the liver is present, and the clinical picture becomes one of septic intoxication. The symptoms of liver abscess are fever, either of the sthenic or hectic type, night sweats, a muddy, septic complexion, local pain in the infrascapular region of the affected side (usually the right), reflected pain in the shoulder, reflex cough from irritation of the diaphragm (unless empyema is present from rupture into the pleura), bulging and edema over the seat of abscess, increased liver dulness in all directions and occasionally swelling of the feet. The duration of the condition may vary from two weeks to several months or, if drainage be established by spontaneous rupture into the lung, for a year. It will eventually terminate in death or recovery through drainage, by spontaneous rupture through the skin or into the bowel or lung. It is extremely doubtful whether absorption of pus ever takes place.

The treatment of intestinal amebiasis divides itself into *prophylaxis* which has been dealt with under the heading of *etiology* and the treatment of the dysenteric and hepatic manifestations. Local treatment is the most important of all measures in amebic dysentery and it is well to disabuse one's mind of the belief that cures are effected by medicines introduced through the mouth. We have to deal with a local inflammatory condition of the colon some thirty feet or more from the mouth and less than one-sixth of that distance, at its remotest point, from the anus. When we admit that we are seeking to produce a local effect on the entamebas in and upon the mucosa of the colon, upon which they are produc-

ing their destructive action, we must also admit that the approach to the seat of the disease via the mouth, esophagus, stomach and through ten yards of intestine is roundabout in the extreme. Our efforts are to be twofold: To dislodge and to destroy the entamebas of dysentery. Theoretically this should be easy of accomplishment, particularly as they are rarely found above the ileocecal valve, but practically the cure of amebic dysentery is difficult and sometimes impossible. The utmost attention to detail and the avoidance of a routine method are essential to good results and it must be admitted that even with the most painstaking and rational effort, failure will too often occur. The attack must be by means of enemata and certain principles are to be kept in mind. We seek to distend the colon, to dislodge amebas, and to bring the amebas in the ulcers and fistulæ as closely into contact with the destructive solution, and for as long a time, as is possible. The pressure, strength of solution and rate of flow cannot be arbitrarily fixed nor can the tolerance of the patient's colon be estimated beforehand.

Temperature and posture will also require variation in individual cases. The knee-chest and the left lateral (Sim's) position are most satisfactory although elevation of the foot of the bed will suffice in some cases where the patients are greatly reduced in strength. This elevation should be about a foot. The medicament to be used by enemata must be one that is destructive to amebas in a strength of solution which will not damage the colon walls.

Experience has proved that quinine is the best agent we have at present for this purpose.

The chief objections to enemata of silver nitrate, salicylic acid, tannic acid, astringents and antiseptics, are on the grounds of pain. Their use has justification from the standpoint of rational practice, but in my experience they are less valuable than quinine by injections.

Quinine enemata should be used warm, at about body temperature, and should be from one to three litres in amount according to the capacity and tolerance of the colon. Recently there has been some argument advanced for the use of ice-cold enemata, it being

suggested that the icy temperature may cause the ameba to assume the encysted form (inactive), thus losing its power to cling to the mucosa, when it may be mechanically removed by the flushing process. Nevertheless, the fact that motile amebas are more readily killed by chemicals than inactive ones and the results of experience lead us to use the quinine solution which should vary in strength from 1:1000 to 1:500, at a temperature of about 100° F. In cases of great irritability it may be necessary to precede these flushings by injections of laudanum (1 to 2 c.c.) or cocaine solution (two percent., small amount) or $\frac{1}{4}$ grain to $\frac{1}{2}$ grain of morphine in warm water, and in *all* cases the quinine enemata should be preceded by large clysters or cleansing enemata of warm water. The quinine injections should be frequently repeated and gently administered through a colon pipe, always bearing in mind the danger of perforation of the ulcerated gut by careless manipulation of the flushing tube. The quinine enemata should be retained for as long a time as possible, fifteen minutes being a suitable length of time. If cinchonism occurs it may be necessary to reduce the strength of solution or give but one enema a day.

The quinine in solution destroys the amebas with which it comes into contact in a manner similar to that in which it destroys malarial parasites in the blood. It probably acts as a protoplasmic poison with a selective action for the protoplasm of amebas.

The similarity of the parasites of malaria and amebic dysentery is not altogether a fanciful one and extends to their biological and structural peculiarities as well as their reaction to quinine, and has been the subject of some investigation by observers of late.

The treatment by massive doses of ipecac has been highly lauded by many writers, but in my experience it has proved to be of no value. It is an uncomfortable ordeal for the patient and is not rational practice. I have seen this method thoroughly tried and I am convinced of its utter uselessness in amebic dysentery and also of its harmfulness. Ipecac in solution has been shown to destroy amebas and if it must be used it should be by the rectal route. Musgrave (p. 103, Bulletin 18, Biological Laboratory,

Manila) states that he has seen three cases postmortem in which ipecac was believed to be the immediate cause of death.

To quote from the same writer (loc. cit.) in connection with the giving of enemata: "In every case all practical methods should be applied to give the largest quantity of fluid which can be administered and retained, for to secure satisfactory results the diseased part of the bowel, which in the majority of cases is clinically the entire colon, must be distended and the fluid retained from five to fifteen minutes." Experience has demonstrated that the danger of rupture of the intestine from overdistension is very small and with a reasonable degree of pressure we may disregard the matter.

An elevation of the reservoir three or four feet above the anus is perfectly safe and in any event the colon must be distended to secure results.

During the two years, 1900–1902, at the United States General Hospital, at San Francisco, "the injection of a strong solution of quinine in amebic cases has been pursued as a routine measure and the treatment has proved most satisfactory, as shown by the physical condition of the patient after the commencement of treatment and by examinations in the laboratory. The amebas quickly disappeared from the feces as did also the blood and mucus; the patients gained in flesh and in the majority of cases rapidly convalesced. Some of the patients, however, after treatment has been discontinued, relapse, and it is again necessary to resume treatment. Taken all in all the treatment by quinine injections in amebic cases has proven the most satisfactory that has yet been tried at the hospital." (The above quotation is from the Surgeon-General's report for 1902.) I was in charge of two wards, of forty beds each, in this hospital from January to April, 1901, and can acquiesce in this verdict.

Another agent which has been used with some success in the local treatment of chronic amebic dysentery is the solution of hydrogen dioxide, U. S. P., given by enema in strength varying from two to ten percent. These enemata may alternate with those of quinine solution with advantage.

Mention should also be made of the surgical treatment of chronic

amebic dysentery which has been seriously proposed and carried out successfully in some cases resistant to the ordinary treatment. It consists of incision into the colon in the hepatic or cecal region, after the organ has been anchored to the anterior belly wall, for the purpose of making colonic irrigations from above downward and securing the flushing of all diseased surfaces with quinine solution or other similar germicidal fluid.

Manifestly this treatment is only to be used in the most intractable cases and after due surgical deliberation. When such artificial opening into the bowel is made it is maintained for the desirable length of time and then closed by operation.

Dietetic, hygienic, tonic and supportant measures have their proper place in the treatment of amebic dysentery and must not be neglected. There should be a careful physical examination of the patient preliminary to treatment, and microscopic examination of the blood and chemical examination of the urine should be made for the guidance of the physician. The patient should be weighed every week and the stools should be examined for amebas every few days, and a record of the findings should be kept. Confinement to bed is not necessary nor desirable except in advanced cases, but the patient should be absolutely under the control of his physician and nurses who should regulate the matters of movement, rest and exercise, diet and the administration of enemata. Some hours of rest in bed each day should be insisted upon and exertion of any kind forbidden. A change of climate, from a tropic to a temperate one, is highly desirable but is not curative of itself. Certain drugs are helpful in certain stages of amebic dysentery. Pepsin and acids for the furthering of gastric digestion, salol and guaiacol carbonate for the prevention of intestinal fermentation and iron for the anemia, are useful in every case. Occasional doses of caster oil or of magnesium sulphate undoubtedly do good, as they dislodge and expose to the action of the quinine solution many amebas which are imbedded in mucus and feces in the colon. Paregoric is useful for pain and it will rarely be necessary to resort to morphine. Alcohol in small amounts is often indicated. The use of bismuth and other

insoluble drugs is not advisable during the period of enemata administration. When, for any reason, enemata are suspended bismuth may be useful to control diarrhea. The guiding thought in the matter of diet should be to provide the maximum of nutriment with the minimum of bowel residue. It is a common practice, but not always a wise one, to insist on a liquid diet. Experience shows that a moderately liberal diet will be borne and will assist in maintaining the patient's strength and resistance to the disease, providing gastric and intestinal digestion are reasonably good. Feedings of measured amounts at intervals of three hours will be found preferable and the patient should never be permitted to eat at a general table or mess.

When this plan is followed there should be occasional days upon which liquid diet only is taken, and castor oil or magnesium sulphate administered. Suppositories of cocaine for irritability of the anus and rectum may be necessary occasionally.

LABORATORY DETECTION.

Organism. Ameba Dysenteriæ; Ameba of Dysentery; Entameba Dysenteriæ. Not differentiable from Ameba Coli, according to Musgrave and Clegg, but according to other observers is a distinct variety of entamebas.

Morphology. A round monocellular protoplasmic body five to thirty-five microns in diameter, colorless or pale green, refractive and showing a nucleus, and at times certain colorless areas resembling vacuoles. (See description under Etiology.)

Motility. Organism has motility but also assumes a resting (encysted) stage under certain conditions of environment. Motility is of variety known as ameboid. (See description under Etiology.)

Cultivation. Has been grown on plate media in pure species by symbiosis with pure cultures of bacteria, but never alone. Methods not available for ordinary laboratory work.

Stains. Takes carbol-fuchsin, methylene blue (Loëffler's stain) and modified Wright's stain well. Also stains in the living state by certain weak neutral stains.

Reproduction. Method of reproduction undecided. Probably by fission or sporulation, or both.

Pathogenesis. Is the cause of amebic dysentery and amebic liver abscess in man and also produces the same diseases (experimentally) in certain domestic animals, cats and dogs.

It is possible and easy to detect the amebas of dysentery in human feces but experience and practice are necessary to differentiate the organisms from certain other bodies present in feces. It is also possible to recover, from a great many sources, amebas which are not distinguishable from the pathogenic ones, but in the present unsettled state of our knowledge we need not seek them outside of the human intestine. Their causal relation to dysentery, when found in dysenteric stools, is established and we can make use of the method of detection for diagnostic purposes.

Method. From a fresh dysenteric stool while still warm, transfer with a platinum loop sterilized in a flame, a small portion or a drop of feces to a cover-glass and drop it upon a clean slide. If the room temperature is low keep the preparation warm by the flame of an alcohol lamp or by the warm stage devised for the purpose. Contrary to the usual advice to select a fragment of mucus for examination, it will be found better to take a drop of the liquid portion of the stool and it will be well to precede examination by the administration of a saline cathartic. This will dislodge many amebas, particularly from the cecal region, and it will make the examination easier and improve the prospects of securing specimens.

The stool examined should be received, when passed, in a clean porcelain bed-pan free from antiseptics or disinfectants. Examine with a one-sixth inch objective or with a lower power for the purpose of picking them up. Look for motile bodies corresponding to the descriptions given above. Particles of fat or globules of fat may attract by their refracting power but the size and nonmotility will quickly clear up the matter. Do not attempt to diagnose amebas unless motility be determined. For comparison with familiar bodies in the feces take the red blood corpuscles.

An ameba will not only be many times larger than the red cell, but it may contain within it from one to six or eight red corpuscles. The clear ectoplasm and the granular endoplasm changing in size, and the ameboid movement by pseudopodia, should all be apparent and particles of pigment and even bacteria may be observed included in the endoplasm. The vacuoles are also apparent and are variable in size. Among the bodies to be differentiated from amebas are large swollen leucocytes and certain smaller monocellular organisms, monads and cercomonads, often present in human feces. These bodies are likewise motile but much more actively so, progressing by flagella and not throwing out pseudopodia. With a little practice and a predetermination to study only motile organisms in the stools one should soon become expert in recognizing entamebas. Examinations for diagnosis should be made with fresh unstained specimens only. If it is desired to study the structure of entamebas they may be studied in the stained state.

Prepare smears by placing together two cover-glasses, upon one of which is the drop or particle of feces, and then sliding them apart. Now place, face up, in equal parts of alcohol and ether and harden for thirty minutes. Dry the cover-glasses and stain at once or later at your convenience. Carbol fuchsin should be used as it stains the nucleus better than methylene blue. Expose the smear to the action of the dye for five or ten minutes and wash thoroughly in water and mount in balsam, after thoroughly drying. The protoplasm will appear to be irregularly stained but the clear ectoplasm and the granular endoplasm are not differentiated. The nucleus, however, will be observed, stained a deep red, situated centrally or eccentrically. Crystalline bodies, possibly absorbed from the feces, may also appear in the stained preparations. Vacuoles appear either as unstained or faintly stained spots. The modified Wright stain recommended by Craig promises to be a most satisfactory one and may lead to the clearing up of the question whether vacuolation is a degenerative or reproductive process.

The procedure in preparing smears of liver abscess pus for

demonstration of amebas, is similar to that of preparing specimens from feces. The cover-glasses should be treated in the same way, two being placed face to face and then drawn apart, thus distributing the pus in an evenly spread layer. It is better not to fix by heat, the alcohol and ether mixture applied for half an hour giving better results. The staining process with carbol fuchsin is in all respects similar to that for intestinal smears. The pus should be taken from the abscess wall and light scrapings thereof may be made with the platinum loop used for transferring to the cover-glass. As has been stated above, about fifty percent. of the liver abscess pus specimens will be found to contain pyogenic micrococci, the result of secondary liver infection.

THE DIAGNOSIS AND TREATMENT OF AMEBIC LIVER ABSCESS.

The diagnosis and treatment of amebic liver abscess is a matter of far too great importance in tropical medicine to be passed over with a word. The condition of suppurative hepatitis, or liver abscess, in the great majority of cases which occur in the tropics, is a manifestation of amebiasis, and while it is not denied that tropical abscesses of the liver may in some cases be due to other causes, among which may be mentioned traumatism, septic infection, typhoid fever, pylephlebitis of appendicitis, and gall-bladder disease, we will confine our remarks to the disease found in intimate association with dysentery or amebic enteritis, and dependent upon the ameba dysenteriæ. Having spoken, in our consideration of amebic dysentery, of the prevalence, pathology and causation of liver abscess, we will now consider the diagnosis and treatment. Cantlie (International Clinics, Vol. 2, Series 14, page 108) divides abscesses in connection with the liver into supra, intra, and subhepatic abscesses, or those upon the upper surface, the interior, and the inferior surface of the gland. Of these three he states that the suprahepatic variety is independent of amebic dysentery and that causes must be looked for elsewhere. Of the intrahepatic variety he states that the cause is usually

dysentery. Of the subhepatic variety he has not encountered cases due to amebic dysentery. This classification does not seem to be of great importance as it is apparent that amebic abscesses may occupy any portion of the liver, and may extend in any direction *within* the organ. In a considerable percentage of the cases the dysenteric manifestations of amebiasis may be in such abeyance, of such trifling character, or so masked that we are without the guiding clue of a recognized amebic enteritis to direct our suspicions to the liver as a possible seat of amebic abscess. In a number of cases the existence of an amebic enteritis has only been discovered postmortem when liver abscess has caused death. The symptoms of liver abscess, therefore, should lead to a suspicion of amebic enteritis, just as the knowledge of amebic dysentery leads us to suspect hepatic abscess. The symptoms may either be vague or definite. The history of dysentery, intermittent fever, a sallow subicteric color, pain in the liver region or referable thereto, swelling and tenderness, make a symptom-complex which is highly suggestive of hepatic abscess, although not absolutely significant of it. Blood study will generally reveal some degree of leucocytosis, the polymorphonuclears being increased, and some anemia, with a decrease in number of the red cells; the leucocytosis becoming more marked as the abscess condition advances. More frequently than otherwise some of these cardinal symptoms will be absent and the symptomatic diagnosis will be far from apparent. We may analyze these cardinal symptoms, and passing over the history of dysentery, we first note the change in color of the patient's skin, which proves to be a cachectic discoloration rather than an icterus, a conclusion borne out by the blood searches which reveal anemic changes. The skin is of a dirty, muddy hue, and the cheeks may show the familiar hectic spots or flush so common in cases of concealed pus accumulations. The scleræ may show some bile staining but are usually abnormally pale.

The temperature curve is apt to be a variable one and of itself gives no accurate clue to the diagnosis. The diurnal variation is from one degree to several degrees, Fahrenheit, and while the

fever is usually intermittent in type, being a degree or two higher at night than in the morning, there may be a continuous elevation above the normal, interrupted by remissions and sweats, either slight or drenching in character. A distinguishing feature of the temperature is its lack of response to quinine. The circumstance of tropical life and exposure to malarial infection, and the not infrequent occurrence of co-existent malaria, dysentery and liver abscess, render it more than likely that the fever of liver abscess will at first be considered malarial. Negative examinations of the blood for malarial parasites and failure of response to quinine should cause the abandonment of this idea. Osler, Manson, and other clinicians agree that cases of liver abscess always appear for diagnosis *after* thorough saturation with quinine. There is usually no splenic swelling in liver abscess unless a complicating malaria be present. The fever may also suggest tuberculosis, typhoid fever or empyema.

Pain in the liver region, or referred pain in other regions, is a valuable symptom in liver abscess. It is rarely absent and is felt in most cases in the liver region, and is dull in character, sometimes throbbing, and at others merely aching. Pleural or peritoneal friction and inflammation usually cause sharp lancinating pains but these do not appear until the disease is well advanced. Most physicians are familiar with the referred pain of the right scapular region, common to acute or chronic liver engorgement. A similar pain is often present in liver abscess, generally on the right side. In many cases there is also referred pain at the point of the shoulder, generally corresponding with the lobe of the liver involved, right or left. Thompson, of the University of Texas, finds this symptom of great value in association with fever and hepatic swelling. Tenderness, or pain elicited by pressure over an abscessed liver, may, or may not be present.

Swelling or enlargement of the liver is probably always present in liver abscess, but on account of the situation of the organ within the bony thoracic cage, it may not always be perceptible. If the enlargement be upward, and of sufficient degree, it will encroach upon the territory of the lung, crowding upward the lower lobe of

that organ. The area of liver dulness will naturally be increased in a vertical direction. If the enlargement is downward there will be a perceptible area of liver dulness below the costal border, anteriorly, particularly if the enlargement is toward the sharp anterior edge of the liver. Bulging outward may be observed below the costal margin in many cases, and encroachment upon the territory of the stomach may also occur.

To distinguish between pleural effusion and an enlarged liver, the patient should be placed on his left side, in which case the level of dulness remains stationary if it be due to a pleural effusion. If it be due to an increase in the volume of the liver the dulness will be decreased by the gravitation of the enlarged right lobe, the compressed lung resuming its normal situation.

An absence of symmetry will be noticeable in most cases and there may be bulging of the intercostal spaces. Fluctuation may even be made out in the bulging areas at times.

The line of liver dulness will rarely be horizontal, and it may extend to the height of the eighth rib posteriorly, or even higher. If the enlargement extends in the direction of the dome of the liver there may be no perceptible frontal enlargement. On the other hand, it may extend to the umbilicus. Accompanying the liver abscess there is generally a wasting of the body, and this wasting makes more apparent the prominence of the epigastric or hypochondriac regions. If the left lobe of the liver be involved, splenic dulness may be simulated. The tape measure may be used to demonstrate the lack of symmetry of the two sides of the body. In some cases percussion over the hepatic areas is distinctly painful, and there may be tender intercostal spots. The sweating in liver abscess cases is usually more pronounced at night than in the daytime, but it may occur at any hour of the day. The tongue will generally be coated, but its appearance will be influenced by the condition of dysentery, usually present, and under certain conditions it may be red, and of a raw, beefy appearance.

Ordinarily there is no albumin in the urine and no distinctive changes occur. Chilliness may be a prominent symptom and

a slight chill generally occurs before the afternoon rise of temperature. Severe rigors may occur at any time, however. Respiratory disturbance is common. The rate may be increased and the respiration may be very shallow, abdominal breathing being quite absent in some cases. Whenever the situation of the abscess is such as to cause irritation or inflammation of the pleura, diaphragm or lung, a reflex cough is excited which is often difficult to control. When the abscess has approached the surface and adhesions to the abdominal wall are present, there may be localized edema and indentations upon pressure. As the case advances the circulation shows the usual evidences of a septic process; the pulse becomes rapid, weak, and perhaps irregular and edema of the legs may occur. If the stethoscope is applied to the chest, the breath sounds over the bases of the lungs, especially over the right lower lobe, are faint and occasionally pleuritic friction sounds are to be heard.

Another sign of liver abscess is rigidity of the abdominal recti muscles. The right rectus, especially, seems to be alert and on guard when the palpating hand or finger approaches the hepatic region. If the patient be observed in a standing position, it will be noted that his body inclines either to the right, or in a forward direction. It may also be noted that a cough, a deep breath, or a jar is painful.

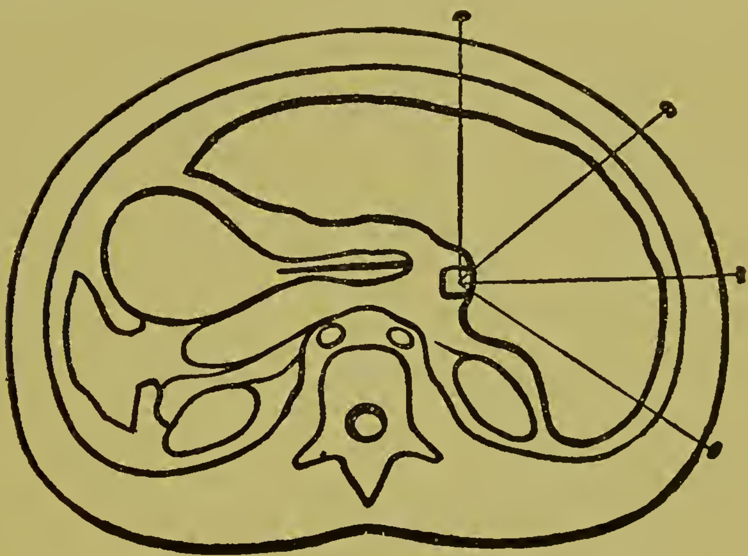
Notwithstanding the fact that some of the signs mentioned will invariably be observed in cases of liver abscess, there is no tropical condition which requires more careful diagnosis, nor any which is more frequently overlooked than tropical liver abscess. Cases are often insidious of onset, and the possibilities of mistaking the condition for some other affection of the upper abdomen or lower thorax are large. Something of a surgical sense, not to be described in words, often leads to the detection of liver abscess, just as it leads to the detection of concealed pus accumulations elsewhere in the body. An important matter is the mental attitude of suspicion. This should always prevail in a locality where dysentery is common, and in the tropics generally. It leads to early diagnosis which is all-important in liver abscess, and which

if properly acted upon, will save life. The chances of spontaneous evacuation of a liver abscess and of natural drainage into the lung or intestine, are comparatively small. Even if it occurs, the probabilities of death from exhaustion are large and no competent or experienced practitioner will advocate a "do-nothing" policy if liver abscess is once demonstrated.

Diagnosis includes a determination of the *location* of pus as well as the fact of its presence, and localizing symptoms should be thoroughly studied before operation is undertaken. Diagnostic procedure includes liver puncture. In the majority of cases it will be quite impossible to make a positive diagnosis of liver abscess (unless it be far advanced and pointing near the surface), without resort to puncture, and it should always be performed before operation, even if diagnosis has been otherwise established. Until pus has been revealed by hepatic puncture there will always be doubt. When an abscess cavity is discovered by puncture the localization is, of course, determined, but often the study of symptoms will direct our explorations successfully. Fear of producing dangerous or fatal concealed hemorrhage frequently prevents the use of the exploring needle. This danger, while not altogether imaginary, is less than is usually supposed. The portal vein may be wounded and cause hemorrhage, but the chief danger is that of puncturing the vena cava. Even this accident is not necessarily fatal, while the failure to discover and drain a liver abscess is practically so. Cantlie has established some anatomical facts which lead to the avoidance of the accident. (International Clinics, loc. cit.) He found by experiment that: "1. The inferior vena cava lies at (practically) equal distances from the chest wall anywhere in the region between the lower end of the sternum in front and the angle of the lower ribs on the right side, that is, the region of operation in liver needling. 2. Given a chest of thirty-two inches circumference at the seat of operation the centre of the inferior vena cava is (practically) everywhere in the area mentioned four and one-half inches distant from the surface. 3. In a chest of greater or less circumference than thirty-two inches the inferior vena cava is deeper or more shallow respect-

ively, but in what exact proportions the writer has not yet had an opportunity of determining. 4. It follows, therefore, that in a chest of thirty-two inches circumference at the level of the liver the puncture needle should not be introduced more deeply than three and three-fourth inches."

The accompanying diagram from Cantlie's article illustrates the situation. It likewise illustrates that deep exploratory puncture of the left side of the chest at this level would be a much more dangerous procedure. Fortunately the right lobe is far oft-



James Cantlie, "International Clinics, 1904."

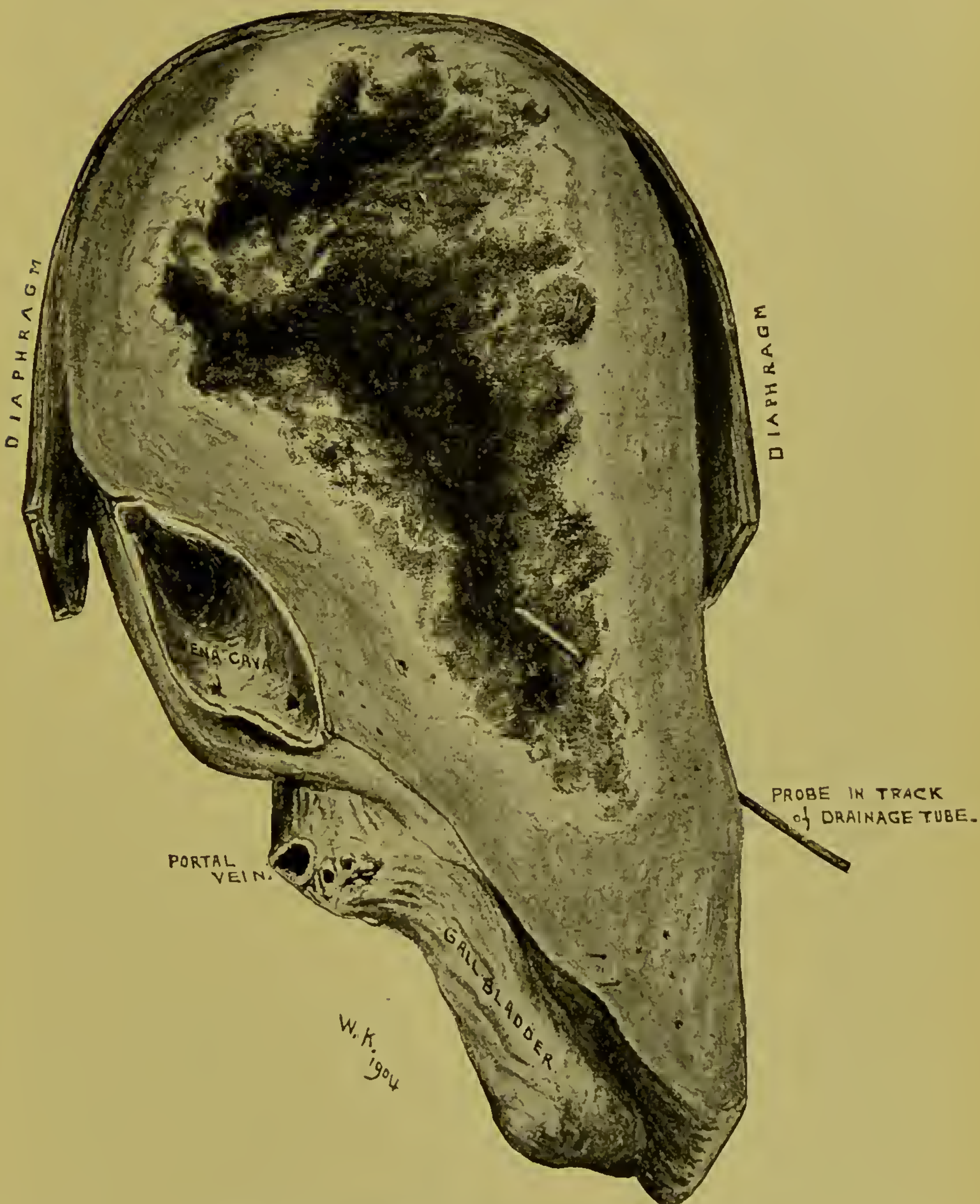
Fig. 35.—Diagram showing the inferior vena cava to be practically equidistant from the surface of the body at the level of the liver, anywhere in a line drawn from the xiphoid cartilage horizontally around the right side of the body as far as the angle of the ribs.

ener primarily involved than any other portion of the liver, although secondary abscesses may completely riddle the gland.

Cantlie also points out that the lowest point of the right pleural sac is about three fingers' breadth above the lower margin of the ribs, and that the lower border of the lungs is about two fingers, breadth above this. In consequence a low intercostal puncture need not necessarily wound either pleura or lung, but if it does will probably produce no bad results. The relief of tension in a congested liver by exploratory puncture, even when pus is not

discovered, is often considerable and is productive of good. The instrument should be sterilized by boiling immediately before using. Several varieties of exploring needles are used. The selection is not of vital importance. An aspiration apparatus should be connected with the needle and it is important that a syringe producing a perfect vacuum be used. Rubber tube connections are not desirable and if possible the syringe and needle should be directly connected and of but two pieces. Sterilization of the skin at each point of puncture should be secured by scrubbing with soap and water, a 1 to 1,000 bichloride of mercury solution, or a carbolic acid solution, followed by alcohol or ether. It should be remembered that aspiration may fail to bring pus, even though an abscess cavity be punctured, if the needle be introduced too rapidly, or if it be of too small calibre. The syringe should have a glass barrel in order that the pus may be seen as soon as an abscess cavity is entered by the needle point. The number of punctures permissible depends upon the condition of the patient and his ability to stand pain, if the exploration be undertaken without anesthesia. It is usually wise to conduct the entire exploration under ether or chloroform, and Manson and Cantlie insist that operation should follow immediately upon the location of pus by aspiration, and that a delay of even a day is not justifiable. This seems to be good teaching based upon sound reasons. Thus, a single period of anesthesia suffices for both exploration and operation, and there is no danger that the abscess cavity located by exploratory puncture will escape the operator or require additional searching for, as is frequently the case when immediate operation is not performed. Six, or even more punctures may be made before desisting if there is good reason to suspect liver abscess. Local edema or bulging, dulness or tenderness, may guide us in introducing the exploring needle. On the other hand there may be no such guides and we may have only the knowledge that liver abscess is generally right-sided and that the cavity is likely to be in the direction of the dome, and somewhat posteriorly. We should remember the depth to which we may safely introduce the trochar and proceed boldly.

Treatment. The treatment of liver abscess consists in evac-



James E. Thompson, "International Clinics, 1904."
Fig. 36.—Extensive single abscess of the liver—amebic.

uation of the contents by operation. Medical treatment is worse

than useless and delayed surgery, after diagnosis is established, is unpardonable.

Operations. A superficial liver abscess, that is, one pointing near the surface, requires simple incision. It does not, however, speak well for the courage or diagnostic skill of the observer, as it must have been central and located well within the substance of the liver at the outset, and it must have consumed considerable time in approaching near enough to the surface to produce the evidences of a superficial abscess.

There may be, of course, exceptional circumstances which will acquit the medical attendant of a lack of diagnostic skill. In the case of a superficial abscess the treatment is simple incision and drainage by gauze packing or rubber tube, generally without irrigation. The adhesions present will prevent the escape of pus into the pleural or abdominal cavities.

When liver abscess is more deeply seated, however, we are obliged to choose between two methods of approach: (1) Through the chest wall or (2) through the abdominal wall. These involve transthoracic section or abdominal section or a drainage operation by means of trocar and cannula.

Let us first consider the matter of *transthoracic section.* If there is bulging between the ribs we may expect the abscess to have for its coverings the diaphragm and the pleural layers. These will require stitching together, in order to prevent the escape of pus into the pleural cavity. A resection of one or two ribs must precede this stitching. This done, the abscess may be opened by an incision through pleura and diaphragm.

Deep-seated abscesses should rarely be approached in this way, as the steps of rib resection, uniting the diaphragmatic and parietal pleural layers, anchoring of the liver to the wound and incision of the hepatic peritoneum, are all preliminary to the search for pus within the liver substance. The situation of the liver at the bottom of a deep recess, its movements to and fro with respiration, hemorrhage and the technical operative difficulties unite to make this a deservedly unpopular operation.

If we approach the liver abscess through the abdominal wall,

the preliminary operation is that of *abdominal section* in the epigastric region. The liver is then to be fixed to the abdominal wall by two rows of stitches through its capsule and peritoneal covering to the edges of the abdominal incision. These stitches should be so placed that the pointing abscess within the liver will correspond to the opening in the abdominal wall. The abdominal incision is kept open by gauze packing and adhesions are permitted to form between the parietal and hepatic peritoneum, the incision of the abscess being deferred until a later time, usually about forty-eight hours afterwards or later.

In some cases the location of the abscess is apparent as soon as the liver is exposed through the abdominal incision and it may be opened immediately, after walling off the operation field from the abdominal cavity by gauze packing; the edges of the abscess cavity may then be stitched about the abdominal incision after the pus has escaped, gauze or tube drainage being used.

It will be seen that all of these operations are such as require surgical judgment, skill and technical facility of a high order, and it is gratifying, therefore, to know that we have a safe method, easy of performance and attended with excellent results, which can be performed unassisted by any capable practitioner of medicine. This operation consists in withdrawing the pus from a deep-seated liver abscess by means of a *trocar and cannula* and of draining the cavity by means of a rubber tube. The only cutting step in the operation is the incision through the skin of perhaps three-quarters of an inch in length, at the point at which the aspirating needle has been introduced. This skin incision is made for the purpose of avoiding bruising of the tissues by the trocar. The method is essentially that of Sir Patrick Manson, and Cantlie successfully operated upon twenty-four out of twenty-eight cases, a percentage of recoveries probably unequalled in any similar series of cases. (Schmits, who operated by means of incision, adhesion formation and abscess incision with the cautery, secured eighteen recoverices out of twenty-one operations.) The usual percentage of mortality varies from forty to seventy-five or eighty percent. To perform the Manson operation a trocar and cannula measuring

about four inches from the point to the hilt of the instrument, and at least three-eighths of an inch in diameter, will be required. Rubber drainage tubing, of the diameter of the cannula and a foot or more in length will also be required. Thompson, of Galveston, Texas, used the ordinary Emmet ovariotomy trocar and cannula. Having located the abscess by exploratory puncture and aspiration, the trocar and cannula are introduced either in the track of the withdrawn aspirating needle, or, better perhaps, immediately beside it, the aspirating needle, in situ, serving as a guide whereby to introduce the trocar. The skin incision of three-fourths of an inch, previously mentioned, is first made at the point where it is proposed to introduce the trocar. After pushing the trocar and cannula to a sufficient depth to strike the abscess cavity, withdraw the trocar alone. The flow of pus demonstrates that the abscess cavity has been tapped, and this flow should now be checked before the cavity is entirely drained. Now pass into the cannula a length of rubber tubing equal in diameter (in its unstretched state) to the cannula, and stretched over a stiff wire or metal rod so that it will pass into and through the cannula to the depth of the abscess cavity. The introduced end of the rubber tube should be rendered stiff and closed and capable of stretching by tying it tightly at the end and possibly by introducing and fixing a solid button at the extremity of the tube. Thus the stretching of the tube is permitted over the metal rod or director and the introduction of the rubber tube within the cannula is provided for. The end of the stretched rubber tube is now held by the metal director at the bottom of the abscess cavity. Remove the cannula and allow the external end of the rubber tube to contract, thus causing its diameter to increase and to fill the track caused by the trocar and cannula. The metal director is next withdrawn and the rubber tube is permitted to remain as a permanent drain to the abscess cavity, held in position by its rigidity and the pressure of the tissues about it. It should be of ample length, say eight or ten inches, and fenestrated by two openings near the end of the tube which should lie within the abscess cavity.

The only criticism of this most ingenious method is the possibility

of infecting the outer surface of the rubber drainage tube as we introduce it into the cannula through which liver abscess pus has escaped. As liver abscess frequently contains no pus organisms, this is not a grave danger, and, as a matter of fact, experience shows the method to be eminently practicable. In any cutting operation for liver abscess the possibilities of infection are far greater. Care must be taken to keep the drainage tube in place and the external end of the tube should be united by a glass connection to a long rubber tube leading into a vessel containing an antiseptic solution, the free end of the tube being kept immersed in this solution. Syphon drainage is kept up as long as the discharge indicates a continuance of liver destruction by the abscess process. Then it is allowed to heal and close, drainage by smaller tubes being gradually dispensed with. Surgeons sometimes combine the trocar and cannula method with open operations, but the Manson method described seems to have a wide range of application, is easy to perform, and saves life by the drainage of deep abscesses before extensive destruction of the liver has taken place.

After operation the tube should be kept clear of clots or particles of liver tissue, which impede the escape of pus, and if obstruction of the tube be complete at any time it may be necessary to remove it and re-introduce it; or a counteropening may be made posteriorly.

The question of irrigating liver abscess cavities is an unsettled one. Upon purely surgical principles, it seems advisable to introduce some solution which will destroy pyogenic bacteria which may be present, or the amebas of dysentery which have caused the liver necrosis and are still present. Most American surgeons, I believe, would prefer to take the risk of irrigation and doubtless some of them choose the open operation on this account. Experienced surgeons, not by any means timid, find the necrotic layer lining the abscess cavity, with its varying thickness and its friable, free-bleeding character, an obstacle to thorough curettement of the cavity unless the abscess be sufficiently close to the surface to permit exposure to view, free incision, and a subsequent packing. In cases treated by drainage alone this necrotic layer

gradually separates and is discharged through the tube. If the cavity be deep seated the intervening healthy liver tissue prevents the removal of the necrotic layer by the curette. The danger of hemorrhage is also very great. Inasmuch as most of the amebas are found in these ragged walls, however, it seems to me that an effort to dislodge them by gentle irrigation, or to destroy them in situ by irrigations with quinine solution would be a rational proceeding. A soft return-flow irrigating catheter should be used for the purpose. The principal objection raised against the introduction of fluids to the abscess cavity is the possibility that they may reach the open hepatic veins. This danger may be more theoretic than actual.

If untreated surgically, liver abscess will rupture spontaneously in about one-fourth of all cases, the duration of the case varying from two or three weeks to as many months, or even longer, if practical drainage be spontaneously effected. Occasionally such spontaneous rupture is curative but it is far more often fatal. If the rupture occurs into the pericardium, vena cava or peritoneum a promptly fatal termination may be expected. The symptoms of such rupture will be those of septic pericardial effusion, embolism or general sepsis in the case of the vena cava, and suppurative peritonitis in the case of the peritoneal cavity.

When the bowel is ruptured into there will be dejections of pus and when the stomach is ruptured into, there will almost certainly be vomiting of pus.

When the pleural cavity is invaded, the evidences will be those of pleural effusion or empyema, and when the lung itself is ruptured into, the patient will either expectorate the abscess contents slowly or cough it up by mouthfuls. It may also flood the lungs and produce death or the symptoms of pulmonary edema. According to circumstances the escape of pus into the lung and its expectoration will be either rapid or gradual. If it be a slow process the patient may die from exhaustion, or an abscess of the lung may develop with fatal results from sepsis or hemorrhage. These cases sometimes last for months. A rupture into the pleural cavity may convert itself into one of rupture into the lung,

and frequently the conditions of abscess of the liver, pleural cavity and lung will co-exist.

The importance of early diagnosis and surgical treatment is, therefore, most obvious.

It is also important that liver abscess pus be recognized. It is usually of a characteristic color and appearance when unmixed with bile, feces, stomach contents or bronchial secretions. There is generally present a tinge of blood or a blood-streaked appearance. According to the presence or absence of a mixed infection, the pus will vary in color, showing in mixed infection a green or yellow color. In amebic abscess in which pyogenic infection has not taken place, the pus will be chocolate colored with a decidedly reddish cast. This color is due to the presence of fragmented liver tissue, the results of necrosis. There are present, in addition to this granular detritus, both amebas and leucocytes. If bacterial infection be present there will also be micrococci and an increased number of polymorphonuclear leucocytes. In consistence the pus will vary according to the degree of liquefaction, large cavities containing thin liquid pus, while in smaller cavities the pus is thick and sticky and flows less readily.

It has been stated that the treatment of liver abscess is purely surgical but the postoperative medical treatment and the husbanding of the patient's strength are important in the extreme. The cases of spontaneous rupture into the lungs or pleural cavities also require particularly careful nursing. A disadvantageous circumstance is the crippled condition of the liver itself. In many cases so little healthy liver tissue remains that the important function of the organ, to a large extent, must be unperformed. This makes the ultimate prognosis accordingly unfavorable. It is, moreover, a deficiency in the metabolic process which we are unable to supply or correct. Gastric and intestinal digestion may be well performed but assimilation is faulty and imperfect and vital energy is not stored up.

In some cases the associated intestinal amebiasis and the condition of gastric catarrh make the feeding of the patient difficult.

The persistence of fever after operation suggests the probability of multiple abscesses, some of which have not been drained, and is an indication for further explorations.

Aside from the postoperative details of maintaining drainage of liver abscess, by whatever operation it be established, the treatment includes the administration of tonic drugs, aperients, or appropriate treatment for amebic dysentery if it still be present.

The permanent removal of the patient from a tropic to a temperate climate has often been insisted upon as necessary, but it should be remembered that there is nothing curative in such a journey, and, however desirable, it is not an essential part of the treatment. Just as a patient suffering from malarial disease carries his malaria parasites with him, so the sufferer from amebic dysentery, or amebic abscess, carries with him the amebas which have wrought his undoing. The tonic effects of a sea voyage are not to be despised, but neither are they to be expected to cure amebic dysentery or abscess of the liver. The subsequent habits of a convalescent subject of liver abscess should be closely supervised. Alcoholic excesses and dietary intemperance may promptly cause disaster. The consciousness of a damaged liver should always be present and cause the patient to avoid all indulgence calculated to throw extra work upon the crippled organ. The regeneration of liver tissue destroyed by amebic abscess is a subject concerning which we have no definite information as yet, but, as is well known, prolonged suppuration, fever, and general malnutrition promote both fatty and lardaceous degeneration, not only of the liver but of the spleen and kidneys also.

I believe iron, in appropriate dosage and preparation, to be the most acceptable drug for use following hepatic suppuration and operation. Its constipating effects must be guarded against. Exposure to cold, or to conditions likely to produce engorgement or congestion of the liver should be carefully avoided.

A more exhaustive discussion of the surgical treatment of liver abscess is beyond the scope of this work, and the student is referred to two excellent articles in Vol. II, Series 14, International Clinics, by Cantlie and Thompson (to both of which I have

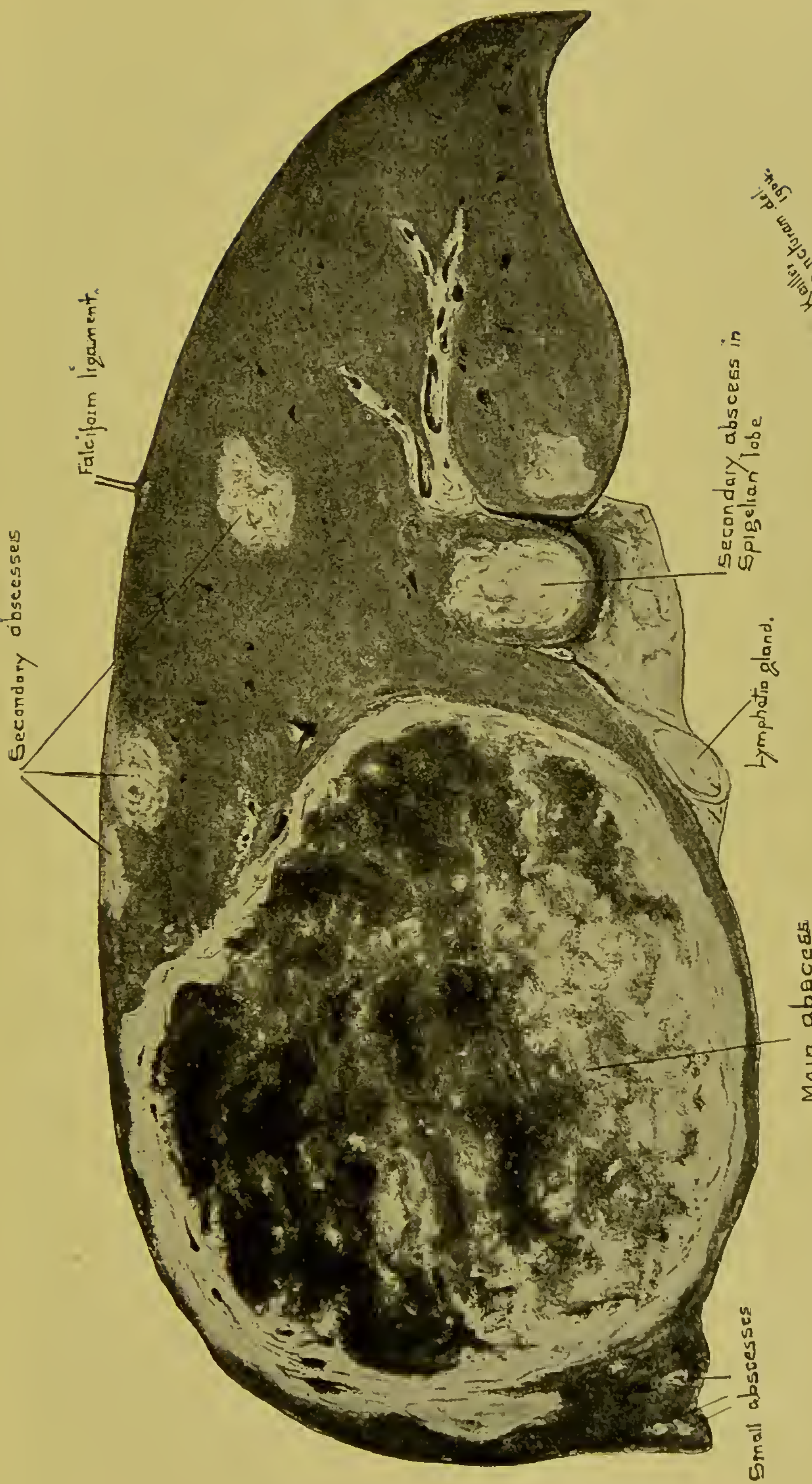


Fig. 37.—Multiple liver abscesses—amebic. (James E. Thompson, "International Clinics, 1904.")

made reference) for a more complete discussion of the surgical aspect of liver abscess, and also to standard surgical text-books.

A word concerning the status of liver abscess surgery in the American tropics may be permitted. Naturally, our military surgeons in eight years of tropical practice have acquired an experience of value, but it can scarcely be claimed to approach that of the English whose tropical possessions, encircling the globe, provide a great wealth of material from which experience is gained, and has been accumulating for years. From my personal acquaintance with American army surgeons I am inclined to believe that their operative experiences in liver abscess have been chiefly with the more formidable operations of abdominal and thoracic section, and that the Manson operation, which I have described, has not been extensively practised.

In Manila and San Francisco numerous operations for liver abscess have been performed each year and the results have been excellent. T. L. Rhoads, Captain and Assistant Surgeon, United States Army, operated extensively and successfully both in Manila and San Francisco, and C. F. Craig, Lieutenant and Assistant Surgeon, United States Army, has added much to our knowledge of the pathology of amebic liver abscess. Rhoads and Craig show from their clinical and pathological observations respectively, that liver abscess in American soldiers occured in about five percent. of the cases of intestinal amebiasis, a circumstance which I have already referred to. The report of the Surgeon-General, United States Army, for 1905, showed an incidence of twenty cases with four deaths, a creditable showing both as to numbers and mortality.

J. M. Banister, Major and Surgeon, United States Army, in the Journal of the American Medical Association, April 30, 1904, writes as follows concerning his experiences with hepatic abscess in Manila in 1903.

"Abscess of the liver is a great bugbear in the tropics, but at the First Reserve Hospital, with a very wide area of territory from which to draw our clinical material, we have only had six patients with this disease during the past twelve months. One patient was operated on twice; once under general anesthesia by aspiration

in the attempt to locate the abscess, and the last time by the abdominal route with evacuation of the abscess. In this case aspiration utterly failed to show the presence of pus, although this procedure was most carefully performed through several different punctures. These six patients were subjected to operation, one by the thoracic route, after resection of a rib, and the remaining five by the abdominal route. A previous history of amebic dysentery was the rule in these cases. There were two deaths in these six cases, in both of which the abscesses were multiple and very extensive. In the four patients who recovered, the abscesses were single, though, as a rule, large. From my own observation and from conversation with other surgeons relative to liver abscess in this climate, I have formed the opinion that with a patient not moribund, and with a single abscess to contend with, a careful operation, either by the thoracic or abdominal route, will afford a very favorable prognosis. In cases of multiple abscesses the prognosis is very gloomy, as patients so affected almost invariably die. Of these six patients suffering from hepatic abscess two were natives. I am especially interested in the fact that two natives were victims of the disease, as I remember reading a short while since in one of the medical journals, published in the United States, that liver abscess was unknown among the natives of the Philippine Islands."

BACILLARY DYSENTERY.

Synonyms. Acute Specific Infectious Dysentery; Diphtheritic Dysentery.

Definition. Bacillary dysentery is an acute, infectious, epidemic disease due to a specific micro-organism, the bacillus dysenteriæ (Shiga), and characterized by a local inflammatory condition of the colon resulting in necrosis, ulceration and sloughing of the mucosa, and by the systemic evidences of toxemia due to the absorption of toxic products of the bacillus dysenteriæ. It is particularly prevalent in tropic countries but also occurs in epidemic form in various parts of the world, including the United

States. It is attended with a high mortality rate. A chronic stage of the disease also occurs.

Facts of Geography and History. In approaching the consideration of Specific Infectious Dysentery we at once encounter difficulties due to the scanty literature extant upon the subject and the brief period of time during which this affection has been recognized as a distinct disease entity. The literature of dysentery previous to 1898 comprised many volumes, written in many languages, and references to a disease which was probably dysentery occurs in Eber's papyrus, written not later than 1500 B. C. Hippocrates, Herodotus, Galen and most of the ancient and medieval writers refer to or describe it with more or less accuracy and it has been the theme of discourse for most of the modern medical writers. The confusion which existed in regard to classification and causation was universal, however, and but little attempt was made to differentiate epidemic dysentery into the two great classes now generally recognized. In consequence of this confusion this mass of literature is of small value to us in a study of the modern disease.

It is well established that specific infectious dysentery is a disease of widespread distribution. Indeed, the geography of dysentery is the geography of the world, and it will probably be demonstrated that this statement is true for the particular variety under consideration.

Since its original discovery and description in Japan in 1898, epidemic specific infectious dysentery has been studied in the Philippine Islands, China, Germany, the United States, Porto Rico and elsewhere, and it is reasonably probable that the epidemic dysentery which prevailed in South Africa during the recent English-Boer War was of the variety now under discussion.

Etiology and Prophylaxis. The earliest important observations were made by the Japanese student Shiga, in 1898, in the laboratory of Kitasato, in Tokyo, Japan. "He reasoned that when the blood serum of a person suffering from, or having suffered from, a certain disease has an agglutinating action upon a certain form of bacteria this organism has probably an intimate connec-

tion with that disease." (Strong, Rept. Surgeon-General, United States Army, 1900, p. 255.) Shiga studied the epidemic form of dysentery prevalent in Japan and from thirty-six cases he obtained a specific bacillus in thirty-four. He named this organism the Bacillus dysenteriæ and arrived, after much study, at the belief that it is the specific cause of epidemic dysentery, at least of the kind prevalent in Japan. He found the bacillus to be a short rod with rounded ends, moderately motile, and resembling most of the bacilli of the colon group and the bacillus typhosus. He did not demonstrate flagella or spore formation and he found that the organism decolorized by Gram's stain. (Strong, loc. cit.)

The blood serum of all of his thirty-four cases gave a positive agglutination reaction for this organism.

Shiga studied the cultural characteristics of the organism and its effect upon the lower animals and also caused to be injected into his own arm a small amount of bouillon culture in which the organism had been killed. He produced in his own serum the agglutinating action for the bacillus, in dilutions of 1 to 10, ten days after inoculation.

This was really the pioneer work in the study of specific infectious dysentery and the observations of Americans in Manila, and in this country, during the subsequent four years were in great degree confirmatory of his conclusions. The principal American workers in this line to whose findings I have had access are: Strong, Musgrave, Flexner, Craig, Duval and Vedder, and I quote freely from their recorded findings and from my own observations in the Philippine Islands.

In an announcement, a few years later than the one quoted, Shiga describes the bacilli as being found almost entirely in the *deeper* layers of the intestinal walls and states that their occurrence is concomitant with the morbid process.

He also states definitely that animals immunized against the bacillus furnish a serum possessing both prophylactic and curative action. (Deut. Med. Wochenshrift, Nov. 7, 1901.)

Flexner, after a comparative study of bacilli isolated by various

observers from cases of dysentery, finds them almost identical, the slight differences depending on accidental circumstances and says: "The results of this comparative study leave no doubt of the identity of the several bacilli with which I have worked. They indicate, moreover, that the acute dysenteries, tending to appear in groups of cases and in epidemics, whether in the Far East, Germany or the West Indies, are due to the same organisms."

He, also, expresses belief that the acute epidemics in this country (United States) are caused by the same organism. (Centr'blt f. Bakt Parasitink. Infectiousk. Bd. XXX, No. 12, 1901.)

"At the 'Institut für Infectione Krankheiten,' Berlin, of which Professor Koch is the director, Martini and Lentz have demonstrated by means of cultures obtained from Shiga, Krause, Strong, Flexner and Pfuhl that the bacilli which were found by these investigators in epidemic dysentery in Japan, Germany, the Philippines, Porto Rico and China are essentially the same." (Salazar, Med. Officer Spanish Army. Anglicized by Barney, United States Army, Journal of Assoc. Mil. Surgeons, March, 1905.)

Additional facts concerning the morphology and cultural characteristics of the bacillus dysenteriæ developed by other observers are as follows: The motility of the organism has not been verified by most observers. Whereas the colon bacillus and typhoid bacillus move freely about from place to place the dysentery bacillus has only a molecular vibratory motion, best seen in the hanging drop preparation. Most observers have failed to demonstrate flagellæ but Vedder and Duval claim to have done so. Bacillus dysenteriæ grows at room temperature, (better in the incubator) in the ordinary culture media, degenerating more quickly in liquids. The cultures are said to yield a slight spermatic odor. Bouillon is clouded, a precipitate but no pellicle forming. Indol is not developed. Bacillus dysenteriæ grows on potatoes as a thin, pale, white, yellowish layer. It does not liquefy gelatine, nor coagulate milk but it makes the latter acid. It does not develop gas in media with lactose or glucose.

There is little doubt that the distribution of the dysentery bacillus is through the medium of dysenteric stools which find their way into water, and thence again into the human intestine to reproduce the disease. Our information concerning the extra-corporeal existence of bacillus dysenteriæ is extremely meager but the method of dissemination is probably in every way similar to that obtaining in cholera and typhoid fever and the clue to prophylaxis is the same as in these two diseases. It is quite probable that flies may play a part in the conveyance of infection, as they do in typhoid and cholera. The prophylactic methods are exactly those advised for cholera and include isolation of dysenteric patients and convalescents, disinfection of the stools and sterilization of the water and food, as well as the protection of food from flies. Perhaps the most dangerous cases, so far as the spreading of the disease is concerned, are those in which the symptoms are mild and the prostration is not sufficiently great to confine the patient to bed, or those in which the chronic stage of the disease has supervened with partial convalescence. These cases are menacing to the community in the same manner that ambulant cases of typhoid fever or cholera are, and emphasize the necessity for early diagnosis of diarrheal diseases, in order that the stools may receive proper disinfection and the freedom of the patient to go about and to scatter the germs of disease, be cut off.

Pathology and Diagnosis. The postmortem appearances in the acute and chronic cases are somewhat different.

The appearance of the intestine in both cases, however, differs markedly from that in Amebic Dysentery, which condition has already been described.

The principal seat of the disease is the *colon.* As in Amebic Dysentery, occasionally the lower six or eight inches of the ileum is involved.

In acute cases the external serous coat of the large bowel may show injection and the lymphatic glands lying close to the upper rectum and sigmoid are swollen, bright red, and on section, hemorrhagic.

Upon opening the intestine the whole of the large bowel, from

cecum to anus, is seen to be involved and the mucous membrane presents a reddened, swollen, puffy appearance with a superficial necrotic layer of mucous membrane which may be wiped away, revealing a bright red, injected condition of the intestinal walls beneath, with small purpuric spots here and there, but without definite ulcerated areas.

The *liver* and *spleen* show no constant changes as a rule but the kidneys may show cloudy swelling. The *stomach* usually shows no distinct changes. The bacillus dysenteriæ has been obtained in pure culture from the hemorrhagic lymphatic glands in a number of acute cases.

In the chronic stage of the disease the picture is somewhat different. The mucosa is no longer bright red. The solitary follicles are swollen, raised and dark red in color. The mucosa is irregularly thickened and while distinct ulcerations are not usual there are superficial erosions and occasionally irregular ulcers of mucosa and submucosa.

Parenchymatous changes in the other organs are more frequent and fatty degeneration of liver and kidneys may be present.

Three varieties of Chronic Specific Dysentery may be recognized, all of them, probably, being different stages of the same process.

They are the *follicular* variety, the *pseudo-diphtheritic* and the *gangrenous* varieties.

The disease begins as the follicular variety and gradually assumes the pseudo-diphtheritic form and later the gangrenous form.

The pseudo-diphtheritic form is believed to be, essentially, a coagulation necrosis with sloughing of the necrosed tissue and the gangrenous form is an intense degree of the pseudo-diphtheritic.

Death is due to pyemia and metastatic abscesses are rather common.

Liver abscesses do not occur, except as metastatic abscesses secondary to pus infections of the ulcerated gut.

Much of the foregoing pathologic description is abstracted from

Strong's report in the Surgeon-General's Annual Report for 1900. To him we owe much of our knowledge of the pathology of bacillary dysentery. The opportunities for autopsy upon dysenteric cases in Manila, in 1899-1901, were exceptional and this advantage was not neglected.

The occurrence of an agglutinating reaction for cultures of the dysentery bacillus is an interesting phenomenon. In dilutions from 1:20 to 1:100, pure cultures of bacilli clump in the presence of blood serum from a patient with the nonamebic variety of tropical dysentery. Animals immunized to the action of bacillus dysenteriæ, by graduated injections, develop the bacteria-clumping property in their sera. This agglutinating principle persists for some time in the blood but does not appear at a sufficiently early period after infection to make it of value for diagnosis, except in undiagnosed chronic cases.

The medical man who has had experience with acute cases of specific infectious dysentery and with cholera infectiosa will not fail to be struck by the points of resemblance in the two diseases.

Both diseases are of bacterial origin, the organism in both cases being similarly conveyed. The incubation periods and onsets are similar and the symptoms and manifestations of toxemia are much alike. In both diseases, the bacteria are practically confined to the intestine, differing in this respect from typhoid fever, in which disease the typhoid bacilli circulate in the blood, producing manifestations at points widely removed from the intestine.

With a knowledge of the symptoms, onset and general characteristics of the disease, the *diagnosis* of specific infectious dysentery should not be difficult although, as in the case of cholera, mistakes are apt to occur during the early days of an epidemic. We have valuable methods of differentiating the disease by the culture of the bacillus, so that it is often possible to positively determine the specific character of an acute dysenteric attack within twenty-four or thirty-six hours. The bacillus must be recovered from the stools, grown and recognized. As in the case of cholera it is sometimes found in almost pure culture in the discharges. The procedures will be found in the section upon

laboratory detection. As has been stated the presence of an agglutinating serum reaction will not be present early enough to be of practical diagnostic value in acute cases.

If the disease has persisted a week or more the serum agglutination test will probably be present. The knowledge that it is usually an epidemic affection and does not often occur sporadically will be helpful.

Some of the diseases with which it may be confounded are Severe Catarrhal Dysentery, Acute Amebic Dysentery, Typhoid Fever with hemorrhage, Asiatic Cholera, Gastro-enteritis, and Ankylostomiasis.

The relative frequency of Amebic and Bacillary Dysentery is a matter difficult of accurate determination. Personally, judging from my own observations, I am inclined to believe that Amebic dysentery is more prevalent in the Philippines than the bacillary variety—except in times of severe epidemics, when the specific variety preponderates.

Of 111 cases of dysentery studied postmortem in Manila, Strong and Musgrave found 79 to be amebic and 32 to be specific (acute and subacute). In another tabulation from the clinical records of the First Reserve Hospital in Manila in 1899–1900, of a total number of 1328 cases of dysentery 561 were amebic and 767 were specific, either acute or subacute.

One attack of bacillary dysentery does not absolutely confer immunity.

Not infrequently the presence of blood in dysenteric stools may be overlooked, minute clots occurring which become coated with mucus and feces and appear only upon close inspection. Such cases are frequently diagnosed as chronic diarrhea. The eggs of ankylostomum duodenale, or the parasite itself, should be sought in the stools when there is a question of diagnosis between dysentery and hook-worm disease. There is no reason why both conditions may not be present at the same time and, in fact, it is rather a common occurrence, but it should be remembered that the conditions are entirely independent. Occasionally it will be necessary to differentiate between typhoid fever and bacil-

lary dysentery. This could hardly be necessary except in subacute or chronic cases of specific dysentery, or at least after the acute symptoms have subsided. If the agglutination tests cannot be made, or if microscopic study of the feces cannot be carried out, judgment must be based upon the history, fever curve, character of stools, and the presence or absence of blood in them. Blood is rarely present in typhoid unless hemorrhage occurs and is fairly constant in dysentery although it may be easily overlooked. Choleriform attacks of malarial disease will occasionally simulate acute dysentery of the specific infectious variety but the differential diagnosis should not present much difficulty. Malarial disease is a common accompaniment of dysentery of all types in the tropics but is to be looked upon as an accidental coincidence and the two diseases are to be independently treated. Under the head of Malarial Disease I shall refer to its intestinal manifestations. (See Chapter VII. p. 292.)

Acute poisoning by certain of the minerals, and cases of ptomain or mushroom poisoning may simulate the acute onset of bacillary dysentery but the differential diagnosis should be easy. The relative absence of gastric symptoms in bacillary dysentery will be a clue. It should not be supposed that the diagnosis between chronic amebic and chronic bacillary dysenteries, from purely clinical symptoms, is easy. Often indeed it will be found impossible unless recourse to the microscopic examination of stools be had. When this is impossible, for any reason, it is wise to assume that an amebic infection exists and to direct treatment along such lines, alternating the quinine enemata with purely antiseptic and astringent ones. While there is no evidence to show that quinine enemata are curative in bacillary dysentery they may prove as effective as some of the weaker germicidal solutions. In chronic cases the agglutination property for the Shiga bacillus will be present in the blood of bacillary dysentery but not in that of amebic dysentery.

Symptoms and Treatment. The incubation period is about twenty-four hours, occasionally shorter than this time and occasionally as long as forty-eight hours.

There are no prodromes, the onset being sudden and often at night, the patient having retired in his usual health.

During the first day, there are frequently as many as forty stools, at first mucous, then bloody and accompanied by great tenesmus. The stools increase in frequency until complete loss of control of the anal sphincters occurs, necessitating the continuous use of the bed-pan.

The discharges may be simply blood streaked or quite bloody, but free bleeding is not usual, and the bowel movements sometimes cease before death occurs.

Fever is *usually* present, of moderate degree, and the tongue is coated with a white fur. The pulse ranges from 100 to 150 and the patient may become algid and die in coma from heart exhaustion.

As in Amebic dysentery, gastric symptoms are often absent. Abdominal tenderness is present over the colon upon pressure but distension is not the rule. Retention of urine is often present *early*, and suppression may occur. Albuminuria is quite a frequent development. Just before death there may occur either rapid elevation or depression of the temperature, with great rapidity and weakness of the pulse.

Most of the fulminant cases die within three or four days but some severe cases survive for ten days.

The symptoms referable to special organs are those of toxemia. The nervous system is profoundly impressed but there is not the extreme restlessness so common in cholera infectiosa. Delirium may develop and coma often precedes death, but convulsions and paralyses do not occur during the disease or as sequellæ. There are no special symptoms referable to the heart or lungs although pneumonias of both varieties have been observed postmortem.

The kidney failure is quite similar to that in cholera, the occurrence of anuria being much less frequent, however.

The vomiting of bacillary dysentery is not to be compared with that of cholera in severity or persistence and, indeed, is often entirely absent. Death does not occur in a few hours as in cholera

and there is never the enormous loss of fluids common to that disease.

The symptoms may gradually abate and convalescence be established within two weeks or the subacute (chronic) stage may develop, with occasional thin, bloody, mucous stools, three to five per day, emaciation and anemia.

The Bacillus dysenteriæ is present, in the acute stage, in the dejecta and in the necrotic layer of the mucous membrane of the intestine.

Leucocytosis may or may not occur and its occurrence, therefore, is not particularly helpful from a diagnostic standpoint.

It will not be out of place here to describe a tropical condition usually considered as a separate disease, and variously known as **Sprue,** Psilosis, and Tropical Aphthæ. There is, it seems to me, insufficient evidence to warrant us in classifying the condition as a distinct disease and it must be admitted, on the other hand, that there is almost as little to justify us in looking upon it as a phase of dysentery. In the present stage of uncertainty about chronic diarrheas and gastro-intestinal catarrhs it will be well to go slowly in accepting statements relating to specific causes, unless convincing evidence accompanies them. The condition is met with somewhat frequently in the tropics and is generally secondary to dysentery or to gastro-enteritis, although it apparently occurs without such history at times. The cause has been variously ascribed to dysentery, enteritis, bad food, malarial disease, the abuse of alcohol and mercury, highly seasoned foods and condiments, hot and cold drinks, and to such indefinite causes as "climatic influence." At different times various animal and bacterial organisms have been found in the stools of patients with "sprue" and have been declared to bear causal relations to the condition but in all cases investigation has proved them to be inconstant and irrelevant to it. The group of symptoms which has been dignified by this name includes serous diarrhea (with an acid reaction), stomatitis, ulcerations of the gums, fissures of the tongue and mucous membrane of the mouth, alteration in the senses of smell and taste, vomiting and other dyspeptic symp-

toms, atrophy of the liver, aphonia, low spirits and even melancholia.

Any of these symptoms may be absent and they may occur in various combinations. The cardinal symptoms insisted upon for diagnosis are the affection of the mouth, gastro-intestinal catarrh, and atrophy of the liver. As remarked elsewhere, all of the cases diagnosed as Psilosis, Sprue or Tropical Aphthæ which I encountered in the Philippines might have been regarded, clinically, as phases of dysentery, or chronic gastro-intestinal catarrh with stomatitis, or as secondary atrophic changes in the entire digestive mucous membrane. I am not aware that anyone has seem fit to venture, even tentatively, the proposition that this degeneration may be the result of the toxic products of the Shiga bacillus. At any rate the consideration of the condition seems proper in connection with dysentery. The treatment is dietetic, tonic and climatic and, as in the case of many degenerations is often unsatisfactory.

English authorities upon tropical diseases, Manson, Duncan, Cantlie and others, lay stress upon the condition of *Sprue* and while, personally, we may be somewhat skeptical as to the identity of the condition, we are bound, it seems to me, to present their views with regard to treatment in a treatise of this character.

The practice of ascribing a condition developing years after one's return from the tropics to previous tropical residence, is most unwise, in my opinion, if there has been an intervening condition of good health. Yet we are informed that "Sprue sometimes commences long—years even—after the patient has returned from abroad." The cardinal symptoms as stated are diarrhea, sore mouth, abdominal distension, and atrophy of the liver, all of a chronic character. The treatment strongly advocated by Manson is that by an absolute milk diet and confinement to bed. He recommends the use of raw milk, undiluted and unboiled, three pints to be given in twenty-four hours at first. The milk is given in divided doses, at intervals of two hours, either from a spoon or through a straw, to provide for its slow ingestion. The feeding is interrupted for six hours at night. Regardless of hunger, this diet

must not be varied from, and no solid food, nor, in fact, any other article of diet, must be permitted. After a few days, half a pint may be added every second day to the allowance until the daily ration equals three quarts.

After each feeding the mouth should be rinsed out with a saturated solution of boric acid in water. The milk is to be given slightly warmed. When three quarts of milk have been taken in twenty-four hours, the patient is permitted to get out of bed. No other article of food, except fresh fruits, is permitted until the stools have been formed and the diarrhea has been absolutely absent for six weeks.

It is admitted that exceptional cases do not get well under this treatment and that milk may require dilution with aerated waters, peptonization, or other modification to suit individual cases. While this treatment may seem to be empiric, its advocates are warm in its praise. We are inclined to believe that many non-tropical conditions of vitiated digestion might be cured by such a rigidly enforced "rest treatment" of the digestive organs, as well as sprue. The resumption of full diet should be most gradual and additions of suitable food should be made daily by the ounce, fish, fowl, mutton, and beef being added in the order named. The entire treatment should occupy six months, exertion and exercise being restricted throughout.

Cantlie, following a similar system of restriction, gives fresh beef juice in place of milk, a teaspoonful at a time, given as often as every fifteen minutes, if required; raw meat, minced beef (three feedings of five ounces daily), calf's foot jelly, steamed pigeon, etc., being gradually added. The central idea is an exclusive meat diet (or nearly so) with hot water as a beverage. The rationale of this treatment is a stimulation to functional activity of the shrunken, atrophied liver. A more rapid improvement and a shorter convalescence are claimed for it by its advocates.

A diet of strawberries, two or more pounds a day, or strawberries in combination with the milk diet, does not appeal to one as being highly rational, yet it also has its advocates.

For relapses (first indicated by sore mouth) induced by indis-

rect diet or chilling, the withdrawal of all food, brief purgation and restoration to milk are recommended.

There is a phase of infectious dysentery which has great interest for nontropical practitioners, particularly such as practise medicine in the great population centres in the summer time. It may be accepted as proved that the infantile epidemic diarrheal disease long known as "cholera infantum" is *infantile infectious dysentery caused by the bacillus dysenteriæ.* It should not be understood that every summer diarrhea due to indigestion and fermentation is to be so classed. It is of the cholera-like variety, long known for its intensity, suddenness and high mortality, that this observation holds good, with some milder cases of enteritis corresponding to the lighter forms of bacillary dysentery which occurs in adults. In the large cities of the United States, New York, Philadelphia, Boston and Baltimore, independent and systematic studies of infantile dysentery were made by Duval and Basset, Martha Wollstein, Howland and La Fêtra, Cordes, Amberg, Warfield, Knox, Hastings, Freeman and Reed in the summers of 1902, 1903 and 1904, the number of cases studied extending into the hundreds. The result of this work has been summarized by Flexner and by Holt and there is great unanimity in the conclusions reached, at least concerning the rôle played by bacillus dysenteriæ in the causation of epidemic infantile dysentery in the great cities of the United States. (See Journal of the American Medical Association for Dec. 17 and 24, 1904.)

The very volume of the literature upon the *treatment* of dysentery bears evidence of the unsatisfactory status of this most important matter. Pages upon pages have been written upon the drug treatment of the disease, very little distinction, if any, being made as to the variety of dysentery for which a special drug is recommended. The truth of the matter is that all systems of medication are wofully wanting when weighed in the balance of rational practice and satisfactory results. The prophylactic side of treatment is well understood and effective. Given control of conditions, the medical man should be able to protect himself and his charges from infectious dysentery. The principles and

the practical methods have already been recited in our studies of cholera and amebic dysentery and do not require repetition.

All prophylaxis, however, must be systematic and unrelenting and the medical man must have the moral courage to withstand ridicule and even abuse from the very persons he seeks to safeguard and to quietly fight on until his cause is won. After all, it is no less laudable to prevent disease than to cure it.

"Most laboratory animals are very sensitive to the injections into the tissues or veins of cultures, living or dead." (Bacillus dysenteriæ.) "Immunized animals develop the agglutinins in the blood. The outlook for a curative serum is encouraging." (Williams, Manual of Bacteriology, p. 315.)

The last statement represents fairly well the status præsens of the serum treatment of infectious dysentery in the United States. In the series of infantile cases, previously referred to, treatment with antitoxic serum was tried in eighty-three cases. To quote from the summary by Holt (Journal of Amer. Med. Assoc., Dec. 24, 1904): "In all there were eighty-three cases in which the antidysenteric serum was employed. Thirty-eight of these were fatal. On the whole the results were disappointing. No unfavorable symptoms followed its use in any case. * * * * In only twelve cases did a noteworthy improvement appear to follow its administration. A careful study of the cases in which the serum was used does not make the results quite so bad as at first appears." He then proceeds to show that: "Several factors worked against success. In a large proportion of cases it was used late in the disease. Again it was, as a rule, used only in the most severe cases; and, finally, at the beginning of the season no rules had been formulated as to the size and frequency of doses, hence it is evident that many of the doses were too small. Four cases were moribund at the time the serum was given. Of the eighty-three cases sixty-seven were hospital patients, and all familiar with hospitals for infants know the class of patients referred to."

In contrast with this series of cases Kruse reports upon the effect of serum used in 100 of his cases (Deut. Med. Woch., Jan. 1–15, 1903) showing a mortality of but eight percent. Of

his 100 cases 3 were moribund when injected and 19 were under 10 years of age. It has been shown that there are probably two strains of the dysentery bacillus in the United States—identical in their pathogenesis but differing in certain minor respects—the Flexner-Harris type which ferments mannite with acid production, and the true Shiga organism. Either one or both of these strains were found in all of the American cases of infantile infectious dysentery and the serum used in the American cases was prepared from both strains. As it is impossible to distinguish clinically between dysentery caused by the two strains, it has been suggested that it would be well to use serum from animals immunized against both types. Further experimentation will be necessary to enable us to form an accurate judgment of the value of serum for prophylactic or curative use.

The empiric method of treatment has long been the prevailing one in dysentery of all kinds but it should be abandoned in the specific infectious variety at least, the cause of which is known. Drug treatment must be conducted with several ends in view, viz.: To render the soil (the intestinal mucosa) upon which dysentery bacilli live and produce their toxins as untenable for them as possible; to destroy them in situ and to remove them mechanically from the intestine; to combat the effect of toxin absorption systemically; to further the repair of all tissues damaged by bacilli or toxins; to further blood construction in the anemia attendant upon and subsequent to infectious dysentery; to relieve pain.

Any drugs which do good in infectious dysentery must accomplish it in one of these ways. The most popular methods of treating dysentery in the British tropics are by saline aperients and by ipecacuanha. Glowing reports as to the efficacy of these methods lead us to believe that the cases reported are certainly not of the variety now under consideration, nor of the amebic variety. Personally my experiences and observations in the Eastern and Western tropics convince me that this is true, and we can only accept such roseate reports with the understanding that very many, at least, of the cases reported are of the simple catarrhal

variety. As stated at the beginning of this chapter this variety of dysentery is not peculiarly tropical and is not under consideration in this work. W. T. Buchanan (British Med. Journal, Sep. 20, 1902) reports that he has the notes of 1130 cases of dysentery treated by the sulphates of magnesium and sodium. These cases occurred in India with a mortality of less than one percent. (nine deaths) and he states that in his last 272 cases no deaths occurred. It is manifestly impossible that these were cases of specific infectious dysentery.

In the Philippines these methods, by salines and by ipecacuanha, were extensively used and the mortality rate for all cases has never approached this low figure, to say nothing of the military discharges for disability incident to dysentery. The treatment by salines consists in administering dram doses of sodium sulphate or magnesium sulphate every fifteen minutes until gentle purgation is produced, and then maintaining purgation until a day or two after mucus and blood disappear from the stools. The treatment should stop short of the production of watery stools, copious soft feculent stools being the test of success by the sulphate treatment, according to Buchanan. (Manson's Tropical Diseases, p. 404.) He recommends the following prescription.

℞ Magnesii Sulphatis .... ℥ii=60. grams.
Acid Sulphurici dil. .... ʒiii=12. c.c.
Tinct. Zingiber.................... ʒiii=12. c.c.
Aquam ad........................ ℥viii=240. c.c.
Sig.:—One or two teaspoonfuls every hour or two until free purgation is produced.

Of all the purely drug treatments advocated I am inclined to give this method, in combination with the use of intestinal antiseptics first place.

Scheube's judgment, based upon experiences in China and Japan, concerning the value of ipecac in varieties of dysentery other than catarrhal has my hearty endorsement. (Diseases of Warm Countries, p. 477, Sheube.) He says: "Though calomel and ipecac have a positive effect in catarrhal dysentery they have

but little effect in the gangrenous form and according to my opinion the same is the case in chronic dysentery." As the excepted cases (gangrenous and chronic) come under the heads of either amebic or bacillary dysentery he practically admits that it is useless in these forms. Having personally used ipecac and observed its uselessness in amebic and specific infectious cases I want to register a protest against its use on the grounds that it is not humane. One who has witnessed the ipecac treatment upon some helpless emaciated dysenteric will not forget the sight. The patient, flat upon his back with an ice bag upon his head and a mustard plaster upon the epigastrium, with saliva pouring from his mouth, fearful to move a muscle, concentrates all of his energy in the effort to repress vomiting, knowing that the dose will be repeated if he yields to the terrible nausea and desire to vomit. It is a sorry picture indeed. This torture is undergone for some hours and perhaps repeated for a number of days. It is not surprising that after such ordeals without particular benefit, patients curse the doctors, nurses, and most of all, the inventors of this modern species of torture.

The details of the ipecac treatment are as follows: After an absolute fast of six hours give 1 c.c. of Tincture of Opium in 15 c.c. of water. After 30 minutes give 30 to 60 grains (2 to 4 grams) of powdered ipecac, in pill, bolus or capsule. Place the patient flat on the back and prohibit eating, drinking, speaking or moving for from four to six hours. Place a mustard plaster over the stomach and an ice cap to the head. The saliva must not be swallowed but wiped from the mouth by a nurse. If the dose is vomited within an hour it must be repeated when vomiting subsides. Repeat the treatment once or twice a day for four days.

The advocates of calomel, especially the Germans, administer it in doses of five grains (.325) every six or eight hours or give it in small doses every hour. Castor oil and Tincture of opium are much given in all forms of dysentery and are of value in allaying tenesmus and profuse diarrhea.

Suppositories of cocaine or opium may be resorted to for tenesmus. Heat, applied to the abdomen in the form of hot-water

bags, turpentine stupes or hot dry flannels, is comforting to the patient, as is the hot bath or the hot wet pack. Ice poultices or ice bags often allay pain when heat fails.

Morphine, by needle, is often required and should not be withheld when indicated, as it serves a double purpose in quieting pain and putting the intestine into a state of rest.

The antiseptic treatment of bacillary dysentery, aside from the irrigation of the colon by antiseptic fluids, includes the administration by mouth of drugs destructive to bacteria, either in solution or otherwise. The difficulties in securing a local antiseptic action in the colon by drugs given by mouth have been explained in the section on the treatment of amebic dysentery. Yet we may hope and seek to accomplish something along these lines.

Salol, guaiacol carbonate, zinc sulpho-carbolate and iodoform are probably the best drugs for use in this way. They may be combined with opium or Dover's powder, tannic acid or other astringents, calomel, bismuth subnitrate, salicylate or subgallate, and pancreatin, and are best given in capsules. When treatment by enemata is being used it is better to omit the bismuth salts. Occasional or daily doses of the aperient sulphates (magnesium or sodium), or of castor oil, should be used to prevent constipation or gaseous distension.

In giving enemata in bacillary dysentery the same precautions must be taken as were advised in the treatment of the amebic variety. Distension of the colon, with as prolonged contact of the medicament with the diseased mucosa as possible, are essential. To secure these ends posture, proper elevation of the reservoir, a suitable colon pipe for delivering the solution and a temperature about that of the body must be provided. Often these local measures do great good, particularly in the subacute stages of the disease, and cures result, the disease showing less tendency to relapse than the amebic variety of dysentery. Sometimes, however, the condition progresses to the gangrenous stage in spite of treatment. The solutions most used for colon irrigation in specific infectious dysentery are astringent antiseptic ones. Preceding the medicated enema a cleansing enema of

normal salt solution, or of a two percent. solution of Bicarbonate of soda, should be given. Nitrate of Silver solution (twenty grains to the pint) may be given in amounts of three to six pints, but often produces considerable pain and local reaction and occasionally these effects entirely preclude its use. It should be followed immediately after expulsion by an enema of normal salt solution. Bichloride of Mercury (1:5000) enemata are occasionally permissible but as a rule very weak creolin solutions will serve better and are less toxic. Solutions of hydrogen dioxide, as advised for amebic dysentery, are useful. The use of olive oil by enemata, either plain or medicated, is advised in the acute stage of specific infectious dysentery. It is sedative and is better borne than astringents and antiseptics. Owing to difficulty in securing pure oil in sufficient amount Ford used it at Washington Barracks (Report of the Surgeon-General, 1904, p. 88) suspended in fresh warm milk (30 c.c. to 60 c.c. of oil to 1000 c.c. of milk), recently agitated. He reported favorably upon its sedative action. It will often be found well to vary the kind and strength of enemata, from time to time, as the avoidance of routine is very desirable in the treatment of dysentery while attention to the details of local treatment is very important. Each case must be separately judged and treated. The matter of *diet* has an important bearing upon the treatment of bacillary dysentery but in this matter, likewise, we must avoid routine practice. Individual peculiarities of case and person must be studied and dealt with. During the acute stage, all foods which leave an intestinal residue should be practically suspended. Egg albumen water, liquid preparations of beef, and other meat broths, barley water, liquid peptonoids and similar preparations, may be given at brief intervals and in small amounts. Later, as the symptoms abate in severity, foods of greater consistence—but always in small amounts and at intervals of a few hours only—may be permitted.

Milk, peptonized or given with Vichy, junket, gelatine, or some of the prepared infant foods may be added and toasted stale bread or "zweibach," ship's biscuit, boiled rice, and poached eggs may be given. Fruit juices and jellies may often be permitted.

Occasionally a more liberal diet of plain, easily digested solid foods will be found to agree better with the patient than liquids or semi-liquid articles of diet. During the acute stages, absolute rest in bed and the use of the bed-pan are imperative, but during the subacute stages the patient should be permitted to sit up, drive, and to have mental diversion, but always under medical supervision. Cold bathing should not be permitted and warm clothing is indicated. Alcohol should be judiciously used in the form of sherry wine or whiskey and it will be well to administer from 2 to 5 grains of powdered pepsin, in capsule, and from 5 to 10 minims of dilute hydrochloric acid (.3 to .6 c.c.) when food is taken. The antianemic measures to be taken include the administration of iron, in sufficient doses, and strychnine $\frac{1}{30}$ grain three times daily with $\frac{1}{60}$ of a grain of Arsenious Acid. Fresh Blaud's pill will be found to be an available and excellent preparation of iron and may be given in five grain doses three times a day. The daily use of castor oil, ℥ i to ℥ ij, will overcome the constipating effect of the iron.

A change of climate almost always benefits the patient but care should be taken that the transition from a warm to a cool climate be gradually made and that the patient be unusually safeguarded from cold by warm clothing. Pneumonias, contracted from exposure, are particularly fatal in dysenterics and great care must be exercised in traveling. In leaving the tropics it is usually necessary to travel by sea and the tonic effect of the voyage is usually marked unless the patient be bed-ridden. A prolonged sea voyage will usually bring the patient to his destination improved but it may also cause the death of bed-ridden patients. Deaths from dysentery at sea were quite common in the United States Army transport service between Manila and San Francisco and I have seen cases die within a few hours after arrival at the hospital in San Francisco, after a month at sea. Doubtless the desire to reach home has buoyed up many a chronic dysenteric through the month's voyage, only to permit him to die in his native land among his friends.

In concluding the discussion of tropical dysentery I wish to

say that I am aware that my treatment of the subject has not been orthodox, according to the teachings of most of the textbooks upon tropical disease. In editions of standard works as recent as 1904 appear statements that our knowledge of dysenteric diseases so far as causation is concerned is practically nil and that anything like a scientific discussion is impossible. American workers in tropical medicine do not share this opinion and I have endeavored to reflect their views, as well as my own, in venturing the classification I have used. It has seemed to me that the volume and the character of research done in the past eight years, and the unanimity of the conclusions of men working in widely separated parts of the world, and under diverse conditions, justify our adoption of their views. If subsequent developments modify some particular view, tentatively advanced, no harm will be done. Dogmatism is an evil to be especially avoided in teaching any advanced views in medicine, but it is also possible to be dogmatic in refusing to accept views that have been scientifically proved.

LABORATORY DETECTION OF THE DYSENTERY BACILLUS.

BACILLUS DYSENTERY.—(SHIGA.)

Name.	Bacillus Dysenteriæ.
Found.	In the stools and intestines of patients with specific infectious dysentery.
Morphology.	A short rod with rounded ends of the size and shape of the typhoid and colon bacilli. Most observers fail to demonstrate flagellæ. Does not form spores.
Motility.	Debatable. Probably has a vibratory molecular motion.
Cultural Characteristics.	Grows on the usual culture media at room temperature but better in the incubator, more slowly than bacillus coli communis. On gelatine plates the growths are whitish and do not liquefy the gelatine. In bouillon cultures a cloudy condition develops

but no pellicle forms on the surface. No indol is produced and no gas is formed in media with glucose or lactose. On potato the growth is thin, pale, and whitish or yellowish in color.

Stains. Stains with the ordinary aniline dyes and decolorizes by Gram's stain.

Pathogenesis. Causes specific infectious dysentery in man.

The principal important facts concerning the bacillus of dysentery are recited in the section on Etiology and are summarized in the above tabulation. What most immediately concerns us is a method by means of which the Shiga bacillus may be promptly recovered from the stools and recognized by cultural peculiarities, for purposes of early diagnosis. Its resemblance to the colon bacillus and to the typhoid bacillus renders its identification by microscopic examination alone less reliable than when verified by cultivation. The characteristics which have been depended upon for differentiating it from the colon and typhoid bacilli are its lack of motility and flagellæ. Both of these points, however, have been in dispute, but it is certain that the motility of the dysentery bacillus, if it exists, is very different in kind from that of the typhoid organism. Bacillus dysenteriæ degenerates and dies easily, particularly in liquid cultures and it resists disinfection but slightly. It dies in the stools in forty-eight hours and in milk and pure water in about a week. In earth it lives about two weeks and in clothing slightly longer. Sunlight destroys it readily and weak solutions of antiseptics soon kill the bacilli, boiling of course immediately destroying them. Unfortunately, few of these destructive agents can operate within the intestine where Bacillus dysenteriæ has its habitat and where it often persists for a long time in the subacute cases. It is frequently present in almost pure culture in acute cases but it is often difficult to recover in the stools of subacute cases. As in amebic dysentery, under similar circumstances, a saline purgative should be given before the search is made.

To cultivate Bacillus dysenteriæ from feces, inoculate agar

plates and incubate for twenty-four hours at 37° C. Any colonies which develop within that time are apt to be colon bacilli, which are often more numerous than dysentery bacilli. Mark their position by pencil upon the glass. Plant the colonies which appear later in dextrose agar. If they develop gas the organism is not the bacillus dysenteriæ. If no gas is developed study further by cultural and microscopic tests and by the agglutination reaction. (Method described by Williams, p. 314, Manual of Bacteriology.) The quick method described by Salazar (loc. cit.) is as follows: Wash particles of mucus in sterile water and then sow them upon a special plate culture medium, consisting of the ordinary agar medium to which is added neutrose, lactose, and tornasol blue. Incubate the plates at 37° C. for twenty-four hours and examine. Colon bacilli colonies appear red, as the colon bacillus forms lactic acid from the lactose and this turns the tornasol blue to red. Both typhoid and dysentery bacilli colonies remain blue and they can easily be differentiated by their motility in hanging drop preparations, the typhoid bacillus being actively motile and the dysentery bacillus being doubtfully motile if at all. The cultures may also be tested for agglutination with the serum of patients with specific dysentery or typhoid, or with the serum of immunized animals. This method of laboratory detection is an exceptionally useful one and easily performed and permits us to determine within thirty-six hours whether or not a given case is one of bacillary dysentery. As has been observed before, the bacilli are not always easily dislodged from the intestinal wall and consequently a single negative finding should not make us too sure that the bacillus dysenteriæ is not present.

CHAPTER VI.

LEPROSY.

Synonyms. *Lepra, Spedalskhed; Leontiasis; Elephantiasis des Grecs;* and numerous appelations of purely local significance.

Definition. Leprosy is an exceedingly chronic, infectious and contagious disease of man, due to the presence and proliferation in his tissues of the *lepra bacillus* (Hansen). This specific micro-organism gives rise to the formation in human tissues, particularly the skin, of nodular masses which subsequently ulcerate and break down; to infiltration and destruction of nerve tissue, both trunk and peripheral nerves, with resultant areas of anesthesia and atrophy; and trophic changes which often terminate in atrophic deformities or the actual loss of various extremities. The disease is also attended by visceral infiltration, by distressing ulceration of the soft tissues, and the loss of the special senses. It is practically always fatal but may extend over a long period of years.

Leprosy is classed with the infectious granulomatous diseases and is clinically divided into three varieties: Nodular leprosy, Nerve leprosy, and Mixed leprosy. A more recently suggested classification divides the disease into Hypertrophic leprosy, including those cases with tubercles, nodules and plate-like masses of new tissue; and Atrophic leprosy, including the cases with anesthetic patches, scars, glossing of the skin, and the wasting of extremities, as for example, the toes or fingers. A Mixed variety is also recognized. Mixed leprosy, under both classifications, includes the cases in which the symptoms of both the other varieties are blended.

While formerly distributed over the Earth without special regard to latitude, leprosy has come to be one of the tropic or subtropic diseases of today, less, perhaps, on account of temperature

and climatic conditions than upon social conditions of living. Segregation of lepers, as carried out in Europe for centuries past, has served, practically, to extinguish leprosy among the Caucasian peoples (with a few exceptions), while lack of general recognition of its contagious character and the close personal contact of daily life common among scantily clad tropic dwellers, have served to keep the disease alive among them. The present-day weight of opinion indicates that leprosy is not an hereditary disease—or at least but doubtfully so—and that while the disease is distinctly contagious, transmission by contact does not readily take place. In view of these favorable facts, prompt diagnosis and life-long segregation of all the lepers in a community should soon cause the disease to disappear, that is to say, within a few generations at most.

Facts of History and Geography. The disease is believed to have been prevalent and widely diffused throughout Egypt, Syria, India and China from a very early date and ancient Indian records, and the early Biblical narrative, indicate that leprosy was known to the ancients and was disseminated, among other ways, by the migrations of the Jewish people. There is great probability, however, that in far less ancient accounts of the disease, syphilis and tuberculosis were frequently confounded with leprosy.

Such confusion probably obtained among the Romans and Greeks and, as a matter of truth, it must be admitted that we have little authentic record of leprosy anterior to the Christian era. It probably appeared in southern Europe shortly before the birth of Christ and during the first ten centuries Anno Domini it certainly became distributed throughout the greater part of Europe and Great Britain, being still further disseminated, in common with other plagues, by the wanderings of the religious hordes of the Crusades. A few centuries later, during the early Middle Ages, the powerful European religious orders, and royalty itself, became so impressed with the prevalence and the devastating character of leprosy that they established hospitals for the unfortunate victims of the disease, and, grasping, in a general way, the contagious character of the malady, instituted the practice

of isolation or segregation, to which institution Europe is indebted for its present-day freedom from leprosy and lepers. The famous order of Saint Lazarus, founded by the Saint of that name who devoted his life to the comfort and service of lepers and died of the disease, was instrumental in caring for thousands of the sufferers.

In time the hospitals and retreats became known as lazarets or lazarettos and the lepers themselves became known as "lazzari" in Italy and Southern Europe, from their patron saint Lazarus.

In the north of Europe leprosy began to abate in the fifteenth century and in southern Europe about two centuries later. It disappeared from Great Britain about 1742, the last cases occurring in the Shetland Islands. Morrow states that the last leper, a Shetland Islander, died in the Edinburgh Infirmary in 1798. At the present time the disease is most prevalent in Asia and the East Indies, although present to some extent throughout Africa, South America, Australia and certain of the Pacific Islands.

In India and China leprosy cases are found in the greatest numbers, but Japan, the Malay Peninsula, the Dutch East Indies and the Philippine Islands all present numerous cases. In 1897 more than 20,000 lepers were reported as living in Japan, and in the Philippine Islands, at the present time (1906) the number of lepers is variously estimated at from 5000 to 10,000. In Europe, the states of the southern tier, Italy, France, Spain and Portugal, all contain a number of endemic cases, but aside from Norway and Russia, most of the northern European States, including the British Isles, are free from all except a few imported cases. Norway is the chief distributing depot for leprosy for Europe and certain parts of the United States, notably Minnesota, where Norwegian emigrants have introduced the disease. In the United States there is also a leper centre in Louisiana which is at least thirty years old. Numerous cases of imported leprosy, usually in the persons of Chinamen, are found in most of the great cities of America. Cuba, Central America, Mexico and most of the South American States furnish cases, some imported ones in the persons of Asiatics and some native cases. The Hawaiian Islands

are notorious for the prevalence of leprosy and the leper colony at Molokai (Hawaiian Islands) has furnished us with much information concerning the disease.

Apparently, leprosy was introduced into the Sandwich Islands about 1850 and at times the disease has shown as great a prevalence, in the native population, as one case in every thirty native residents. At present the disease is waning, owing to the segregation of all lepers, and it bids fair to disappear within a generation or so. In Africa the disease extends from the northern states, Morocco, Tripoli, Algiers and Egypt, to Cape Colony. In the Philippine Islands leprosy is widely distributed, without particular reference to locality, altitude, or proximity to the coast. According to observations in Manila, where new cases are being constantly admitted to the leper hospital, it is not possible, as yet, to state whether the disease is becoming more or less prevalent. In a large proportion of the lepers admitted, the cases are of long standing, some giving a history of ten years' duration. The natives (Malays) resist or oppose the efforts to segregate sufferers from the disease, and doubtless many cases are concealed.

The following abstract from the Journal of the American Medical Association for Aug. 26, 1905, calls attention to the present situation, as regards leprosy, in a certain province in China, and being from an official report, it is interesting as reflecting the popular estimation in which the disease is held and the absolute unconcern of the people of the affected province. This particular province of China was also the starting point for the present great pandemic of bubonic plague, and it is admitted that pest has been endemic in Yunnan for thirty years or more, without giving rise to any great concern upon the part of the populace or authorities. These facts point strongly to the necessity for an Occidental sanitary invasion of the filthy Eastern centres of population, which have for years supplied us with diseases which only fail to ravage our people by reason of our civilized condition and the general observance of sanitary laws.

"The Public Health and Marine-Hospital Service calls attention to a medical report, by Dr. Georges Brarbezieux, in the

publication of the Chinese Imperial Customs, in which is described a remarkable focus of leprosy existing in Yunnan, the most southwest province of China. The report states that the number of lepers is very great and that they wander in the fields and about the streets of towns, frequenting abandoned pagodas and presenting the horrible stigmata of the disease. There are in Yunnan entire villages of lepers where the inhabitants live miserably on the products of rice fields. These persons have slight relations with the outside world, though they are free from the restraint of sanitary regulations and are not by any means ostracized. Nevertheless, they seclude themselves from the society of healthy persons, mingle with lepers only, and do not visit other villages except when the gravity of their disease renders labor impossible. When broken down physically by the progress of the disease they join themselves to more prosperous and healthy communities, and thus swell the immense army that lives in such places by public charity.

"With the advent of white men in Yunnan the number of leprous beggars has notably increased. It is estimated that in Yunnan there is one leper for every hundred inhabitants, but the concentration in certain parts of the country is still greater than the general figures indicate. There are no institutions, public or private, for the care of these unfortunates, and the disease is not considered to be more than very slightly, if at all, contagious."

Etiology and Prophylaxis. In taking up the consideration of causes we immediately group the etiological factors as predisposing and exciting, and with the positive knowledge at hand of the part played by *bacillus lepræ* we group all the factors except Hansen's bacillus into the predisposing causes. The usual predisponents of sex, occupation and climate may be set down as negative in effect, except in so far as they conduce to contagion. The contagiousness of leprosy has been established reasonably well and may be passed here with the comment suggested by Sternberg ("Infection and Immunity") that "it would otherwise be difficult to conceive as to how the disease is propagated."

A recent observation concerning the contagiousness of leprosy

is contained in the official report to the British Colonial Office in regard to leprosy in Basutoland, just published. (American Medicine, July 29, 1905, p. 202, Vol. X, No. V.)

In 148 studied cases 68 persons have a history of more or less close association with lepers prior to the appearance of the disease in their own persons. In 50 of these individuals close intercourse was shown, while 4 persons claim that they contracted leprosy by sleeping for a single night in places where lepers were quartered. In all the other cases the patients denied intercourse with lepers.

We cannot discard the idea that leprosy is in some way communicated from the sick to the well although we are still somewhat in the dark as to the exact method of conveyance. It is alleged that nodular leprosy is more common in cold climates and that the anesthetic or nerve variety occurs more frequently in warm dry climates but it also appears that wherever the disease occurs, and it is nearly world-wide in its distribution, both forms are common. Observations as to the age at which the disease appears indicate that it is most common between the ages of ten and thirty years, although it may appear as early as the first year and as late as the fortieth year. It is rarely seen, however, before the fifth year. The observations of H. B. Wilkinson, Physician-in-Charge of the San Lazaro Hospital in Manila (Journal of the American Medical Association, Feb. 3, 1906), and others, tend to convince that the disease is rarely, if ever, transmitted from parent to child and that where several cases occur in a single family we should look for a common source of infection rather than hereditary transmission. Manson pertinently states that: "Since the discovery of the bacillus it is impossible any longer, if we properly consider it, to believe that the bacillus itself, and therefore the disease it causes, can be hereditary in the scientific sense of the word 'hereditary.' Physiological peculiarities and susceptibilities may, but parasites cannot, be inherited. It is true that the ovum may be infected by a germ, as in syphilis; but infection is not heredity." (Tropical Diseases, p. 510.)

Of the exciting cause, the lepra bacillus, discovered by the Norwegian, A. Hansen in 187~~0~~, and subsequently accepted every-

where as the causative organism of leprosy, we will speak more fully in the closing section of the chapter, describing its principal morphologic features and methods for its recovery and identification.

One of the most suggestive theories of transmission is that of contagion through the secretions of the nose and mouth and primary infection through a lesion of the mucosa of the respiratory or digestive tracts, with secondary systemic invasion through the blood and lymph channels. Morrow contends by argument and observations that this is the usual method of infection. (Twentieth Century Practice of Medicine.)

Leloir calls attention to the fact that the Norwegian peasant is very dirty and his statements of actual conditions among the Norwegian peasantry, among whom leprosy is common, are perfectly compatible with the theory just stated, and, indeed, support it. The Norwegian peasant, he remarks, rarely if ever bathes during life, except the hands, face and feet; the face and hands weekly and the feet annually. Woolen clothing is worn and never washed and is discarded when too rotten for further wear. Otherwise it is passed from one generation to another. Promiscuous living, several sleeping in a single bed, among the most disgusting conditions of filth and the accumulated excrement of men and animals, is common, and a common spoon, drinking vessel and dish are used by all in a household.

The same is true regarding eating and drinking among the native Hawaiians and in addition they pass a common pipe from mouth to mouth, bite from a portion of food, such as meat or fish, and pass the remainder to the next. They also drink a beverage (ava), in the preparation of which, the root, from which the drink is made, is chewed by others. (Observations of Mr. Meyer, Superintendent of the leper colony at Molokai, H. I.) While we are not, perhaps, justified in looking upon this suggested method of inoculation as the only one, or even as the usual one, the presence in the secretions referred to of myriads of lepra bacilli, the common occurrence of ulcerations of the nasal mucosa in lepers, and (by analogy) the similarity of leprosy to syphilis and tuberculosis,

two diseases conveyed in this identical manner, are sufficient reasons for us to consider carefully this theory of communication. Inoculations of blood, pus and leprous tissue containing lepra bacilli have been negative for man, except in a few doubtful cases where individuals of a leprous family, or otherwise exposed to contagion, have developed the disease. Typical leprous nodules, with recovery therefrom of lepra bacilli, were produced by inoculation in two monkeys, according to Nicolle ("Acad. des Sci.," Feb. 20, 1905).

The determination of these matters is rendered difficult by the long period of latency, generally admitted to occur, which follows infection in at least many cases of leprosy.

The popular fear of lepers is unwarranted in the light of our modern knowledge of leprosy and there is little danger that the disease will ever spread in countries where the people are cleanly and observe sanitary ways of living, as, for example, in the United States. The ultrasanitary manner of life of the cultured and wealthy is not even essential. Common cleanliness and wholesome living will suffice to prevent the spread of leprosy. Individual imported cases may now and then occur and, for the good of the whole community, the victim should be kindly but forcibly isolated. Leprosy is so feebly contagious, or as Manson expresses it, the conditions for successful contagion so rarely occur, that it might, perhaps, be possible and safe to abandon isolation in countries where civilization is on a high plane, and to insist only upon restricted intercourse, frequent disinfection of the body and the destruction of the bacilli-bearing excretions. It is certainly true that both syphilis and tuberculosis are far more readily communicated than leprosy. Unfortunately, however, the latter disease is practically incurable and almost invariably fatal. At present and, indeed, until the manner of transmission of leprosy is definitely determined, it would be inexpedient to abandon segregation or isolation. In view of the facts that leprosy is not hereditary, as formerly believed, and also that sexual desire and procreative ability are diminished and often absent in lepers, colonizing the unfortunates seems to be the most humane and

practical method of dealing with them. In parts of Europe and the United States cases of leprosy are now treated in hospital wards, usually as contagious cases, without apparent evil results. Owing to the conditions of life in tropic countries generally, it is unsafe to advocate this plan of procedure there. International health authorities advocate and enforce isolation and colonization and at present no less rigorous policy seems advisable. In the United States various propositions, looking toward the State control of lepers, have been presented to the various legislatures at different times within recent years, and the National government itself has recently been solicited to undertake the establishment of a reservation for the leper population of the entire country and its insular possessions. An argument against the institution of leper colonies by the various individual states, which has been advanced by the people, is that such provision would be apt to attract lepers from states without such retreats, to residence in the states where asylum and treatment are provided, in order to secure to them the right to admission and treatment. In view of the limited number of cases scattered through the various states Federal control seems to be the preferable plan. Concerning such Federal control, American Medicine (Dec. 10, 1904, p. 988) says editorially: "Objections to any remedial legislation that may be secured will no doubt arise. No state will welcome the proposed sanitarium." According to the private records of Dr. Ashmead there were (in 1904) 143 cases of leprosy in New York and 400 in Louisiana. Continuing, the editorial quoted states: "Legislators should be enlightened regarding the gravity of an affection that may remain endemic in a country for scores, or even hundreds of years, and then, assuming epidemic characters, spread with frightful rapidity. In Colombia, South America, 40 years ago there were 400 lepers. Now there are 30,000. Surely the people of this country should welcome governmental efforts to suppress such a disease, even if the measures adopted are in a sense distasteful; against such measures no argument save that of absolute danger by contamination need be seriously considered." In connection with the subject of leprosy in Colombia, South America,

the announcement of Dr. Juan Carrasquilla of Bogota, in a pamphlet published by Hernando Santos of Bogota in 1905, is surprising and difficult to harmonize with the facts observed elsewhere by other students of leprosy. (Journal American Med. Assoc., Vol. XV, p. 499, 1905.) Dr. Carrasquilla has enjoyed a reputation extending beyond Colombia, for his efforts to cultivate the lepra bacillus and to prepare an effective curative serum, in both of which attempts it is claimed that he has achieved a certain degree of success. In this announcement Dr. Carrasquilla expresses his disbelief in the contagious character of leprosy and also his conviction that the intermediation of vermin is essential for the transmission of lepra bacilli and that the infection is transmitted by vermin. While Carrasquilla's teaching concerning cleanliness of body and habitation and protection against vermin is admirable, on general principles, his conclusions concerning the method of transmission and the noncontagiousness of leprosy are certainly not acceptable to students of the disease in the absence of specific demonstration.

Pathology. The tissues of the body showing pathologic changes in leprosy are various and include the nerves, skin, viscera (the liver, spleen and kidneys), the mucous membrane, cartilages, and, according to some authorities, the bones. The lymphatic glands and testes, when affected by leprosy, contain the lepra bacilli and occasionally they are found in the blood and may even be observed included by leucocytes. The brain, lungs, spinal cord, and the intestinal tract rarely contain lepra bacilli, or at least the organisms are infrequently demonstrated there. The changes in the tissues are due to the multiplication of the invading bacillus lepræ and to irritation caused by its products; and these changes include infiltration and the growth of granulomatous tissue of lymphoid and epitheliod elements. Distributed throughout the leprous tissues, either discretely or in colony-like masses, are found the lepra bacilli. The typical leprous lesions are the results of this growth, plus infection with pyogenic micrococci, and local death. The gross lesions will vary according to the anatomic structure invaded and will be described briefly and

separately. We will first consider the two tissues most commonly affected in leprosy, the skin and the nerves.

The earliest *skin* manifestations of leprosy are erythematous patches, rose or pale violet in hue and later becoming brownish and pigmented, which resemble the roseola of macular syphilis.

Fig. 38.—Macular Leprosy. (Van Harlingen, Diseases of the Skin.)

Successive crops may appear and finally become permanent. This form of lepride is usually symmetric and appears on the face, extensor aspects of the limbs, hands and feet. Macular leprides of various shapes, and size, increasing by circular extension with paler central areas, may run together, producing geometric pat-

terns upon the skin and frequently resembling ring-worm. This eruption may be limited or extensive. Later on, papules may occur which become nodular after a slow growth. From their earliest appearance, lepra bacilli may be demonstrated in the infiltrated borders of these leprides, by examination of skin sec-

Fig. 39.—Tubercular Leprosy—early stage. (Van Harlingen, Diseases of the Skin.)

tions excised under cocaine anesthesia produced by intradermal injections. The evolution of the nodule from the papule is usually a slow one and when complete we have a tubercle-like mass, varying in size from that of a split pea to that of a good sized nut. This mass, the leproma, consists of a small-celled neoplasm

derived from the infiltration of the deep layers of the true skin. Another form of leproma, derived probably from the flat, macular lepride, is a plate-like elevation of dense tissue measuring some inches across. Up to the time that liquefaction necrosis begins the epidermis is usually unbroken and the leproma varies in color from red to brown, showing pigmentation as a rule. Lepromata

Fig. 40.—Tubercular Leprosy—advanced stage, with ulceration. (Van Harlingen, Diseases of the Skin.)

may appear on almost any part of the body except the scalp, but are rare upon the palmar and plantar aspects of the hands and feet. With the beginning of liquefaction necrosis and the solution of the epidermis, a pus infection may be implanted and ulceration or extensive sloughs may occur. It will be apparent

that confluent lepromata may give rise to obliteration or exaggeration of the natural features and landmarks of the skin and when this occurs upon the face, particularly the eyebrows, forehead, nose, chin and ears, the so-called "leonine" appearance is marked. From this appearance is derived the term "leontiasis," sometimes applied to nodular leprosy of the face. Preservation of the hair of the scalp accentuates the lion-like appearance. The skin over lepromata usually gives a greasy sensation to the touch. Lepromata are well supplied with blood vessels and do not undergo caseation and, according to Hansen, do not contain giant cells. Leproma cells are round cells about the size of a leucocyte and are grouped near the blood vessels. Within them, but never within their nuclei, are found lepra bacilli, often in great abundance. "Globi" are dark, granular bodies, which Hansen believed to be lepra cells in which lepra bacilli had died. Accompanying the facial infiltration, the fingers and toes are apt to take on infiltration and a sausage-like appearance. It should be borne in mind that ulcerations in skin leprosy are not necessarily expressions of the disease. They may result from engrafted pus infections upon a broken integument, and in nerve leprosy they may be the results of atrophic gangrene and pyogenic infection. The usual ending of lepromata is in ulcerative destruction, although central softening with absorption may occur, a smooth patch of scar tissue remaining to mark the site of the nodule. Ulcerating syphilitic gummata and tubercular lesions may resemble leprous ulceration and it is quite possible for the diseases to exist in combination.

Passing to the pathologic changes in the *nerves* we find that the essential process in nerve leprosy is one of neuritis with degeneration and atrophy. In the early stages of change lepra bacilli are present and demonstrable in the cells and also in and between the nerve fibres. In the secondary inflammatory changes, such as fusiform enlargements of nerve trunks, the bacilli may not be found. Nerve leprosy begins as a perineuritis and the affected nerves appear red and swollen but later lose their redness, becoming gray and firm, and nodules and fusiform swellings appear.

Under the microscope granular infiltration with lepra and lymphoid cells, and thickening, are usually observed in the neurilemma.

Pressure upon the nerve and interrupted nutrition, cause contraction and destruction of function and in time the nerve fibres disappear, fibroid hyperplasia causing the trunks to resemble fibrous cords.

The view that neuritic leprous infiltration is originally interstitial, rather than parenchymatous, has also been held by pathologists.

The characteristic anesthesia of nerve leprosy is, of course, incidental to the involvement of the fibres which conduct sensory impulses but there is some reason to believe that this anesthesia begins in the nerve terminals in the skin and extends centrally towards the nerve trunks, the lepra bacilli being found in the tissues around the terminals during the early and incomplete anesthetic symptoms. This is the view of Gerlach and others.

In the upper extremity the ulnar, radial, median and musculo-spiral nerves, and in the lower extremity the anterior tibial, peroneal and external popliteal nerves are especially apt to show leprotic changes and swelling. The great auriculars may also be involved. When superficially placed between the skin and an underlying bone, these enlarged nerves, sometimes as large as pencils and resembling cords, are to be recognized. The swellings are usually fusiform.

In the *central nervous system* certain inconstant changes, expressive of leprosy, or at least coincident with the disease, have been observed.

In a few cases cavity-like lesions have been found, suggestive of syringo-myelia, which, with the anesthetic areas and trophic changes common to both diseases, have caused some confusion as to diagnosis and have even led to claims of identity for the two conditions. The most common pathologic change observed is edema, with an increase of cerebro-spinal fluid and distention of the ventricles and subarachnoid space.

The pathologic changes in the *mucous membrane* in leprosy are similar to those of skin leprosy, the typical lesion being the nodule,

which, later on, may break down. The principal sites of mucous membrane leprosy are the conjunctiva, cornea and the nasal mucosa. The lungs, larynx and trachea are also occasionally invaded and nodular leprosy of the pleura (serous membrane) secondary to pulmonary infection, has also been observed. Leprous nodules appear in the submucosa around the blood vessels, which are gradually obliterated, giving rise to fibrosis. These nodules may soften or ulcerate, from pyogenic infection, or they may remain firm. In the lungs ulceration is less common than in tuberculosis and the nodules resemble miliary tubercles.

In the eyes leprous infiltrations occur in the conjunctiva, cornea and iris, and hardening or ulceration ensues. Paralytic changes from nerve involvement also occur in the lids and ocular muscles.

Visceral leprosy manifests itself in the liver, spleen and kidneys in two ways. Points and lines of a yellowish white new growth, which contain lepra bacilli, are observed in both spleen and liver and, rarely, true nodular leprous masses are found in these organs. In the spleen "nodules of granulation tissue containing lepra cells and loaded with the bacilli in quite characteristic clusters" are found (Coplin, Pathology, p. 441).

Many lepers are nephritic but rarely, if ever, are true leprous nodules or infiltration found in the kidneys. The nephritis is believed rather to be due to the excretion of irritant products of the disease, elaborated elsewhere in the body. Cloudy swelling is evident in these organs in many cases of leprosy.

According to some pathologists, distinct leprous nodules closely resembling tuberculosis occasionally occur in the medullæ of bones. Other authorities deny the existence of bone leprosy.

The disease rarely involves muscles and cartilage, although tracheal and laryngeal lesions occur, by extension from adjacent (mucous membrane) structures. As previously stated, lepra bacilli are occasionally found in the blood, either free in the plasma or included in leucocytes. They also occur in the vessel walls and in lymph glands adjacent to structures showing leprous infiltration. The glands are swollen and infiltrated and contain lepra cells and bacilli. Upon section they are firm and of a yellow-

LEPRA TUBEROSA.

This photograph of an Italian leper woman who lived in New York City, undiscovered, for a long time, is reproduced through the courtesy of Dr. William S. Gottheil, Dermatologist to the City Hospital, Blackwell's Island, New York City.

ish color. Atrophy of the testicles is the rule in male lepers and these organs may also become infiltrated and may contain lepra cells and bacilli.

Symptoms and Treatment. Although it is customary in describing leprosy, as with other diseases, to divide it into definite clinical stages, as, for example, the stages of infection and incubation, prodromes, macular eruptions, leprous deposits and sequellæ, there is in fact little warrant for so doing. These arbitrary stages are so imperfectly separated, one period merging into the next, or indeed several periods apparently coinciding, that the attempt to so divide them will not be made. Concerning the so-called infection and incubation stages, we are practically without definite knowledge, the time elapsing between the instant of possible infection and the well-developed disease varying from a year, or even less, to many years. Essentially the disease is a most protracted one. The average duration of 239 cases now in San Lazaro Hospital, Manila (1906), as given by Wilkinson (loc. cit.) is 8.11 years; 77 lepers have had leprosy for over 10 years; 12 for over 20 years; one for 31 and one for 41 years. Seven lepers have been in this hospital continuously for over 10 years; two for 17 years; and one for 18 years. The classification into nodular, neurotic or anesthetic, and mixed cases; and into hypertrophic, atrophic and mixed cases has already been mentioned. The advantages of both classifications are sufficiently apparent. Of the 239 Manila cases mentioned 97 are grouped as hypertrophic, 47 as atrophic, 92 are mixed forms and 3 are described as undetermined. Twelve cases show no disability; 96 show less than 50 percent. disability; 37 show 50 percent. disability; and 94 show more than 50 percent. disability. The following symptoms, somewhat in the order given, are usual in the early stages of leprosy and are often spoken of as prodromes. They seem to indicate that nerve involvement in leprosy occurs early. Whether or not the production of toxins by the lepra bacilli causes these symptoms is purely speculative. Headache, somnolence, vertigo, perversions of sensation, hyperesthesia, fever, neuralgias, and myalgias, usually intermittent and covering a period of months,

may be noted. Just as local sensibility is at first increased and later disappears, so, also, sweating is at first profuse and exhausting and later disappears, at least over the leprous areas.

In some cases, however, the earliest symptom noted is the macular eruption. The appearance of this macular lepride has already been described, as has been the evolution of the plate-like leprous mass which is believed to be derived from the macule. The papular lepride does not usually appear until after the macular exanthem has shown itself, faded and reappeared, and, as has been

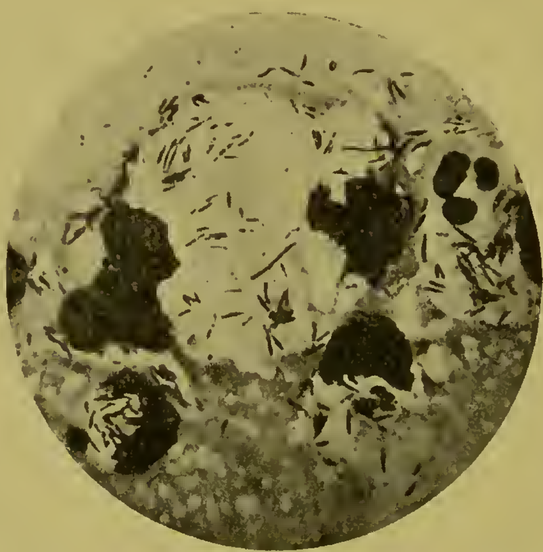


Fig. 41.—Bacillus of leprosy in tissue. (Rosenau.)

shown, this papule develops into the leproma, the typical nodular, infiltrated neoplasm of skin leprosy.

In location the macules seem to elect the face, forehead, extensor surfaces, back, chest and abdomen, avoiding the scalp and hairy parts generally. The eyebrows, however, may be lost and likewise the beard in spots. Concomitantly with the development of anesthesia in the macular areas, there are apt to occur longitudinal strips of anesthesia on the ulnar borders of the arms, on the outer aspects of the thighs, and on the inner borders of the hands and feet. These ribbon-like areas are believed to indicate neuritis of the corresponding nerve trunks. Another manifestation

of anesthesia, believed to indicate spinal leprous lesions, is that of segmental anesthetic areas, extending from the feet or limbs upwards and associated with considerable perversion of sensation as regards location. Clinically this latter form of anesthesia is late, and often but poorly marked. If the macules described do not develop into plate-like masses they may be the sites of pemphigus-like lesions, blisters or bullæ, which rupture, crust over, exfoliate and atrophy into white scar-like spots.

Fig. 42.—Nerve leprosy, showing perforations and mutilation of hands. (Van Harlingen, Diseases of the Skin.)

On the other hand the bullæ may ulcerate, coalesce and form large, raw but superficial sores. Such lesions may heal and crack, become purulent, excavated or finally heal, according to circumstances of pyogenic infection, sloughing, etc. It must be borne in mind that these appearances may persist either months or years. It will suffice to simply enumerate the various symptoms of nerve leprosy which may now develop. Some of them have

already been described under Pathology. They are the results of neuritis, atrophy and local death. The muscles of the forearms and hands, including the interossei muscles, atrophy and the hand assumes the "Main simienne engriffe" appearance; or dry gangrene may amputate fingers or toes. The fingers may become contracted and claw-like. A perforating ulcer of the ball of the foot (a common symptom), may develop and exposed joints, such as elbows and knees, may undergo ulceration, ankylosis or destruction. With the wasting of muscles comes loss of power. The progress of nerve leprosy is generally slower than that of nodular or skin leprosy.

Nodular Leprosy. When the eruptive papules of leprosy have developed into nodules the appearance is usually so characteristic that tubercular or skin leprosy can immediately be diagnosticated. Having described the appearance of the lesions in this form of leprosy in some detail, under Pathology, simple mention of some of the symptoms will be given here. The leonine appearance, the sinking of the nose from destruction of its cartilages, the nodular condition of the tongue and soft palate, the laryngeal involvement affecting the breathing and the voice, the loss of smell and taste, destruction of the eyes, a fetid odor, swelling and possibly suppuration of the glands of the neck and groin, all occur in nodular leprosy. If the lesions and symptoms of nerve leprosy now be added, and many cases are mixed cases, we have a condition horrible to contemplate; one which Manson thus describes:

"Altogether, the blind, lame, unhappy wretch, still retaining his intellect but devoid of every sense except that of hearing, breathing with difficulty through his stenosed larynx and racked by neuralgic pains and irregular outbursts of fever, comes to present before the inevitable death from exhaustion occurs, a sadder, more loathsome, and more repulsive picture than anything imagination could conceive."

Providentially, however, few lepers live to attain this unhappy state, intercurrent disease or organic changes due to visceral leprosy, bringing relief by death.

Treatment. After extended trial and experiment with all the

suggested drug treatments of leprosy, most authorities, particularly the Norwegian students of the disease, including Leloir, agree that no drug with which we may successfully combat leprosy has been brought forward yet. Howsoever melancholy this statement, it seems to be a truth. In a disease so liable to tardy progress, and even to indefinite interruptions, treatment values must be estimated most carefully. Nothing short of the permanent disappearance of the lepra bacilli can be counted as a cure and there is no known drug which either invariably, or with reasonable constancy, produces this result. Nevertheless, we may mention the drugs to which have been accorded the highest virtues and which are most in vogue in the treatment of leprosy. Most favorably regarded, perhaps, is the oil of gynocardium, or Chaulmoogra oil, known and used in China for the treatment of leprosy for centuries. This preparation is unofficial.

It is expressed from the seeds of Gynocardia Odorata and is of an offensive odor. It may be given in capsules in doses of 8 or 10 drops and cautiously increased, if tolerated, to 20 or 30 drops to the dose; the maximum daily amount reaching 200 drops. It is likely to produce gastro-intestinal irritation and may be given in milk. It is also used hypodermatically, or by inunction diluted with oil. By needle, Manson has administered one dram daily while Jeanselme gives 10 c.c. (162 minims) per week in two doses. Gurjun oil, an oleo-resin obtained from certain trees of Southern Asia, has also been similarly used, in doses from ten minims to two drams. Unna advocated the internal use of ichthyol in gram doses, using inunctions or external applications of pyrogallic or chrysophanic acids, in ten percent mixtures with lanoline, upon the local lesions. This plan of treatment is followed for a month and then interrupted by a course of warm baths, following which the treatment is resumed.

Crocker has used, with some benefit, bichloride of mercury in-injections in doses of $\frac{1}{8}$ grain, weekly.

The consensus of opinion with regard to Potassium Iodide in leprosy is that it is distinctly detrimental and injurious. Others have used and advised Salicylate of Soda, Europhen

and Creosote in various doses and ways, and Potassium Chlorate internally in the enormous dosage of fifteen to twenty grams, daily, has been advocated. Tincture of Nux Vomica, Strychnia, and tonics generally have been advised and doubtless do definite good. Cod liver oil and iron, in particular, are useful drugs with which to build up the tissues and the resistant forces of the patient. Experiments with tuberculin go to show that, although its injection produces a delayed local and systemic response, it is followed by an increase in the leprotic eruption and a general aggravation of the disease. Leprolin, to which I have referred elsewhere, has not been thoroughly tested as yet. Concerning the original antileprous serum of Carrasquilla, Le Dantec believes it to be a cytotoxic serum rather than an antitoxic or antimicrobic one. It was prepared by injecting human leper serum into the horse. His second serum, it is claimed, is prepared by injecting cultures of bacillus lepræ into the horse. La Dantec believes this preparation to be obtained from a saprophytic microbe, rather than from the true lepra bacillus, which organism, he contends, has not yet been cultivated. Manson reports a case of nerve leprosy treated with thyroidin as clinically cured.

The surgical treatment of leprosy is deserving of some attention, and will, I believe, receive more serious consideration hereafter. It includes, not only the effort to check or limit the disease by excising early lesions, in the hope that they may really be the initial lesions, but also amputations, surgical operation for the correction of deformities, operations upon diseased bones and cartilages, and the excision of ulcerating areas which are serving as centres for septic poisoning and the undermining of the leper's strength and general health.

It also includes such operations as nerve stretching and the transplantation of tendons and nerves for orthopedic purposes, as well as for the relief of neuralgias. Some of the eye lesions of leprosy are amenable to surgical relief, and it has been observed that lepra bacilli do not pass through corneal cicatrices. Iridectomy and similar operations may be performed to prolong the

preservation of vision. Tracheotomy is sometimes indicated and performed, in leprous stenosis of the larynx. The cautery is frequently used for the destruction of leprotic lesions.

Phototherapy has recently been suggested in the treatment of leprosy and in view of the chemic properties of the ultraviolet rays, successfully utilized in the electric light bath, and of the successful use of Rœntgen rays, in lupus and epithelioma, the proposed treatment seems rational, being based upon the bactericide properties of certain light rays and their demonstrated powers of penetration of the skin, especially when that structure is rendered bloodless, or nearly so. The following facts abstracted from the report of H. B. Wilkinson, Manila (loc. cit.), are the latest and most convincing ones yet advanced in this connection. In the reported cases X (Rœntgen) rays, developed by means of an X-ray machine, were applied to thirteen lepers with the results stated below. The period over which the observation extends is one year and the treatment consisted in exposing the parts of the body showing the greatest amount of leprotic deposit to the X-ray for ten minutes, for each treatment, at a distance of from seven to ten inches. X-ray burns resulted in but two cases. Accompanying the report are photographs showing the condition before and after treatment and clinic, bacteriologic, and pathologic reports.

In one cured case, which died from an intercurrent disease, the pathologic report includes the autopsy record and the government laboratory report of careful section and microscopic examination of the skin and internal organs, disclosing the complete absence of lepra bacilli. In this case the bacilli were abundant in the skin a year before, when X-ray treatment was instituted. Wilkinson's report indicates that of thirteen lepers treated with Rœntgen rays, three were cured, seven were improved and three were not improved. The three cured cases had histories of one and two years' duration of the disease prior to treatment. The seven improved cases varied from four to eighteen years in duration and the three unimproved cases were of from one to nine years' duration. The greatest number of X-ray treatments was fifty-two, given to one

of the cured cases. The smallest number of treatments was eleven, and the result was improvement. Some of the conclusions reached by Wilkinson and his co-workers are as follows: They believe the X-ray kills localized lepra bacilli. These bacilli are absorbed and produce immunity against living bacilli, a parallel immunity to that produced by injecting killed cultures of an organism (as for example plague bacilli) in certain other diseases. In support of this view they urge that the direct treatment of a leprous spot produces improvement in distant spots, as well as in the spot directly exposed. The distant effect seems to be parallel to, and quite as complete as in, the locality directly exposed to the rays. The best results were obtained where the tissues began to show death from exposure to the X-ray (probably causing the death of the lepra bacilli also), and the cases with massive leprous deposits improved most rapidly, probably due to an abundant culture of lepra bacilli in the tissues, and a correspondingly abundant amount of the immunizing principle produced by their destruction.

The leprous American soldier now under the observation of medical officers of the United States Army at Ft. Screven, Ga., concerning whom extended reports upon the effects of treatment by X-rays have appeared in the Annual Reports of the Surgeon-General of United States Army for the past three years, remains uncured. The latest published report, that of 1905, states that the patient feels perfectly well but that a few nodules in the skin and ulcerations in the nose show that the disease persists. This soldier was treated by X-ray treatments, alternating with leprolin injections, and the internal administration of mangrove-bark preparations, and was also subjected to experiments to determine whether or not "the human body could be utilized as a medium for the growth of this organism (lepra bacillus) which had refused to grow in all laboratory media."

For this purpose bacilli-laden tissue fragments from his own body, and also from lepers in the Louisiana colony, were introduced under his skin by surgical operation. The official judgment in his case is that "the results are decidedly favorable and a permanent cure is at least a possibility." Manifestly, any final or

binding conclusion relative to the value of X-ray treatments in leprosy, based upon the records at hand, would be premature, and we can but express the hope that the treatment may prove to be curative. Certainly, the following points in connection with the dosage should be carefully studied, with a view to standardizing experiments or treatments; the amount used, the quality of the tube used (whether of a high or low vacuum), the distance between the tube and the patient, and the length of time and frequency of the treatments. Schamberg calls attention to these points, among others, in connection with the treatment of cutaneous diseases. (Diseases of the Skin, Blakiston, Philadelphia, 1905.)

Before leaving the subject of treatment, mention of the value of hygienic living, in its broadest sense, to the individual leper, must be made. At the present time it is admittedly the most important factor in retarding the progress of the disease, of which we know. In addition to personal cleanliness, and ordinary bathing, vapor bathing with sulphur and arsenical vapors should be ordered and the diet should be carefully supervised, all articles of food apt to produce skin irritations or urticarias, as, for instance, condiments, shell-fish, sausage, cheese, strawberries, etc., being omitted from the dietary. In a word, any measure or device, of external or internal application, hygienic, medical or surgical, calculated to preserve the physiological integrity of the skin and the body of the leper, should be resorted to.

Diagnosis. The diagnosis of leprosy is of exceeding importance and the disease is sufficiently definite in its manifestations to permit early identification, if a little more than ordinary care and a watchful expectancy be maintained. Its distribution, as has been shown, is by no means limited to the tropics or the subtropics, and therefore the same watchful expectancy is an appropriate attitude everywhere, and especially in the great cities and sea-ports. While the manifestations of leprosy are truly said to be protean, it is a fact that leprosy bears a decided clinical likeness to two other systemic diseases, and that the serious mistakes of diagnosis, now as formerly, are made in differentiating leprosy, syphilis and tuberculosis. Within the present year (1906),

there was discovered in a certain Soldier's Home in the United States, an American soldier with a perforating ulcer of the foot in which lepra bacilli were demonstrated, who had served in the Philippines and had been discharged from service for disability ascribed to syphilis. A review of the case proved that there was a definite history of a serpiginous or ring-worm-like eruption during service in the Philippine Islands, which at the time was believed to be the eruption of secondary syphilis and was so diagnosticated. This case serves to point the necessity for more careful diagnosis and the accompanying tabulation is designed in the hope of assisting in differentiating the three diseases.

TABLE OF DIFFERENTIAL DIAGNOSIS BETWEEN LEPROSY, SYPHILIS AND TUBERCULOSIS.

	Leprosy.	Syphilis.	Tuberculosis.
Anesthesia.	A cardinal and early symptom. Often symmetric. Usually complete in leprous macules, especially toward centres.	Not present.	Not present.
Eruptive Skin Lesions.	Skin contains lepra bacilli. Eruption often serpiginous or extending from centres; tends to recur and become permanent. Resembles syphilis and ring-worm. Most common on extensor aspects.	Skin contains neither lepra bacilli nor tubercle bacilli. Secondary macular lesions are more evanescent and disappear under specific treatment. Papulosquamous syphilides sometimes resemble leprides, but do not contain lepra bacilli. More common on flexor aspects.	Uncommon. Skin contains tubercle bacilli.
Ulcerating Lesions.	Ulcerating lepromata resemble breaking down gummata Associated with anesthesia, trophic lesions and paretic symptoms. Lepra bacilli present.	Not associated with anesthesia or trophic changes. Lepra bacilli absent.	Tubercle bacilli present.

	LEPROSY.	SYPHILIS.	TUBERCULOSIS.
Pallid Areas.	Common as post-macular conditions. These areas are anesthetic and rarely sweat.	Rare.	Rare.
Facies Leontina.	Common in Leprosy.	Not present.	Not present.
Enlarged Lymphatic Glands.	Common. Contain Lepra cells and bacilli.	Common. Neither Lepra nor Tubercle bacilli present.	Common. Tubercle bacilli present.
Nodular Eruptions.	Resemble Syphilis. Distribution, greasy feeling, presence of lepra bacilli and absence of scalp involvement are distinctive.	Resemble Leprosy. Distribution, absence of lepra bacilli, the history and concurrent symptoms, and therapeutic test serve to identify these lesions.	Tubercle bacilli and tubercular history present.
Thickened Nerve-trunks.	Common. Swellings are often fusiform.	Absent.	Absent.
Fever.	Common precursor of skin and nerve leprosy. Irregular and lasts weeks or months.	Rather uncommon. Usually associated with glandular involvement of secondary syphilis.	Common. Apt to be quotidian and of hectic type.

Pernet discusses the differential diagnosis of syphilis and leprosy in a thorough manner, pointing out its importance from the view-points of the patient and his friends or family, and also of treatment; syphilis, of course, being very amenable and leprosy practicably nonamenable to treatment. (G. Pernet, Diff. Diag. of Syphilitic and Nonsyphilitic Affections of the Skin. Page 139 to 149. Adlard and Son, London, 1904.)

He also emphasizes the desirability of a clinical acquaintance, on the part of all medical men, with leprosy. It should not be possible for any medical student in any of the great cities of the world to say that he has never seen a case of leprosy. In so far as it is possible, leprosy should not be diagnosed by exclusion. The possibility and method of detection of lepra bacilli in every case of leprosy, is dealt with at the end of this chapter, and ultimate diagnosis should include and rest upon the recognition of bacillus

lepræ. The clinical diagnosis of leprosy, however, should not be neglected. On the genitalia a leproma may be mistaken for a chancre, and if it chances to be solitary and associated with glandular induration an erroneous diagnosis of syphilis may easily be made. The leprous lesion, however, is practically always multiple. Reference to the preceding descriptions of leprous lesions, under the head of Pathology, should serve to assist in diagnosis. The objective symptoms pertain chiefly to the skin and nerves and these symptoms have already been described.

The anesthesia of leprosy is so constant a symptom as to be accounted cardinal. It occurs in areas corresponding more or less closely with the leprous skin and nerve terminals, and in the centres of the scar-like, pallid areas, which mark the sites of the macular leprotic eruption, or of absorbed lepromata, anesthesia is complete. In the very earliest stages hyperesthesia is sometimes noted. Leprous anesthesia includes the heat and cold sense, or thermic anesthesia. To test this sense, use two test-tubes, one containing hot, the other cold water. Syringomyelia has been mistaken for, and is apt to be mistaken for leprosy. In the former disease there is thermo-anesthesia and analgesia, in association with wasted muscles, while in leprosy the anesthesia applies to all varieties of sensation and the trophic changes are more marked. Ataxia, loss of sphincter control and spasticity of the legs would be apt to be present in syringomyelia.

Among the skin diseases more or less closely resembling leprosy, but which should be easily differentiated, are erythema nodosum, psoriasis, eczema, ring-worm and lichen planus. Other conditions with nodular, neoplastic or infiltrative swelling are elephantiasis and cheloid. Fever is an early manifestation of the prodromal period of leprosy and precedes, as a rule, definite skin or nerve manifestations. This symptom is especially apt to be disregarded in warm climates. It is quite constant in occurrence but irregular in type and may continue interruptedly for months, and is likely to be mistaken for an expression of malarial diseases. Careful microscopic examinations of the blood for the malarial organism, of course, eliminate this possibility.

Laboratory Detection of Bacillus Lepræ. The causative organism of leprosy, Hansen's bacillus lepræ, is a rod-like micro-organism varying from four to six microns in length and averaging 0.6 μ in thickness. Morphologically, it bears rather a close resemblance to Koch's tubercle bacillus, and a similar likeness, as has been pointed out, extends to some extent to the symptoms and lesions of the two diseases. Bacillus lepræ is almost always straight but may be thicker at one extremity than at the other. Whether or not it is provided with a capsule is a debated question. At times it is granular or beaded in appearance. It occurs in clumps, in which, however, the bacilli are more numerous than in the clusters of bacilli sometimes observed in tuberculosis, and it is found both within and without the lepra cells heretofore described. In the preceding pages its distribution throughout the tissues of the body has been explained. It is demonstrable in most of these tissues. The question of motility is one concerning which a difference of opinion exists, the weight of authority seeming to favor non-motility. Concerning this point Manson says (p. 502): "If examined fresh, or if a morsel of leproma be teased up in water, the bacilli may be seen both inside and outside the cells and in active motion. Whether this motion is simply molecular, or whether it is vital, is hard to say; probably the former, for while osmic acid does not stop it, it is immediately arrested by the addition of viscid fluids, such as glycerine or albumen water."

Bacillus lepræ is generally stated to be uncultivatible in artificial media, but Roth, Van Houtum, Carrasquilla and Spronck claim to have succeeded in cultivating it. Roth used a sodium-chloride-free medium and the others used fish bouillon or meat bouillon. With some of the growths an agglutination reaction with blood serum from lepers was produced, and Carrasquilla obtained a horse blood serum, for which curative properties have been claimed, by injecting filtered cultures into horses. Large numbers of lepers have been attracted to Bogota, Colombia, South America, by his serum treatment. Rost has produced from fluid cultures a "leprolin" which is prepared and used in a manner similar to tuberculin. Reports of cures with this product are recorded.

During 1904 a case of leprosy in the United States Army received a number of leprolin injections without appreciable benefit. (Report of Surgeon-General, United States Army, for 1905, p. 52.) Le Dantec and others express considerable doubt as to the identity of the various organisms which have been cultivated, and there is certainly too little harmony in the experiments and findings to permit us to accept any conclusions as to the cultivatibility of lepra bacilli or the efficacy of leprolin or serum therapy.

Bacillus lepræ is an acid-fast organism and stains in the same manner as does bacillus tuberculosis. It does not decolorize by Gram's stain. Lepra bacilli stained with carbol fuchsin resist decolorization by the mineral acids. Gabbett's decolorizing and counter-staining solution is therefore useful after staining with carbol fuchsin. It also stains by watery solutions of the ordinary aniline dyes. If it be desired to stain the bacilli in situ in the tissues, excision, hardening and sectioning with the microtome will be necessary, but by squeezing a leprous nodule and puncturing with a needle "leper juice" may be obtained, spread upon cover-glasses in films, fixed and stained. The bacilli will be found in these preparations but will be more abundant in smears made from scrapings from the under side of the skin. For these smears a small skin incision over the leproma is necessary. In either case the film or smear should be fixed by passing it quickly through an alcohol flame, and then exposed to a carbol fuchsin solution for three or four minutes. It is not necessary to heat the carbol fuchsin solution as in staining tubule bacilli. Next apply the Gabbett solution for two or three minutes to decolorize and counter-stain. Wash, dry and mount. The lepra bacilli should appear red. All else should be tinged with blue. Slight variations as to the time of exposure to the Gabbett solution may be required to secure satisfactory decolorization. The stained films may be first mounted in water and examined under a $\frac{1}{6}$ lens to determine decolorization. If this is found to be unsatisfactory reapply Gabbett's solution for a minute. When complete mount in Canada balsam. Lepra bacilli may also be demonstrated in the tissues by macerating small fragments of a leprous

nodule in a glass mortar with a few drops of normal salt solution. Spread this emulsion upon cover-glasses, fix and stain as just described. The carbol fuchsin stain may be prepared by adding 10 c.c. of a saturated alcoholic solution of fuchsin to 90 c.c. of a five percent. aqueous solution of carbolic acid.

The Gabbett stain is prepared by adding two grams of methyl blue to 100 c.c. of a twenty-five percent. aqueous solution of sulphuric acid.

In demonstrating lepra bacilli especial care must be taken to avoid the bacilli of tuberculosis, as leprosy and tuberculosis frequently occur in the same individual. The leading features which distinguish *bacillus lepræ* from the tubercle bacillus are its failure to grow upon culture media—at least upon the media which grow tubercle bacilli—and the practical impossibility of producing leprosy in animals. Although, as stated on a preceding page, leprous nodules are said to have been produced experimentally in apes, the disease—so far as our present knowledge extends—is limited to man.

CHAPTER VII.

MALARIAL DISEASE.

Synonyms. Malaria; Malarial Fever; Hemamebiasis; Ague; Paludism; Intermittent Fever; Remittent Fever. *The terms Coast, Jungle, Swamp, Climatic and Paludial, and the names of many cities and countries, when prefixed to the word Fever usually designate Malarial Disease.*

Definition. The condition of malarial disease, or malaria, is one of blood parasitism in man and the term as used here includes the phenomena of fever, cachexia and anemia, when expressions of infection with the protozoal parasite Hemameba Malariæ, which infests human blood and lives in and at the expense of the red corpuscles of the infected individual, resulting in more or less periodic paroxysms of intermittent fever, continued fever or cachexia, according to the multiplication, number and variety of the parasites. The disease is acute and infectious but often becomes chronic.

There is no fact of modern medicine more firmly established than the fact that hemameba malariæ is the sole causative element in the production of this disease and, this being so, a study and knowledge of the parasite are essential to a knowledge and understanding of the disease, particularly as the most notable manifestations of malaria (fevers) are known and have been shown to correspond in type with distinct varieties of the blood parasite. It is further known that man is infected with the hemameba through the agency of the mosquito, which insect acts as the definitive host and carrier of the blood parasite. The parasite has two distinct cycles of existence, one within the mosquito and one within the blood of man, both of which have been thoroughly studied and the facts placed outside of the fields of speculation and presumption.

Facts of Geography and History. The most important historical facts connected with malarial disease are the modern ones. Interesting as it may be to know that Hippocrates described with fair accuracy certain tertian, quartan and continued fevers which were probably malarial, four centuries before Christ, and that Celsus classified the disease still further in the first century of the Christian era, the discoveries of the past quarter century are vastly more important.

In the middle of the Seventeenth Century the Spaniards introduced into Europe a certain Peruvian bark, the administration of which controlled the periodic paroxysms of malarial fever. This bark, Cinchona, named after the Peruvian viceroy, Del Cinchon, was curative for most of the malarial fevers and by its use Juan del Vego, personal physician to the viceroy, was able to discriminate between malarial and nonmalarial fevers. Thus was established the "therapeutic diagnosis," which remains today a diagnostic measure of great value to practitioners cut off from the modern microscopic method.

From the days of Juan del Vego (1640), who discovered a cure for the disease, to those of Laveran (1880), who discovered its cause, the study of malarial disease was marked by no achievement of similar importance. The last twenty-five years, however, has witnessed great activity of investigation and such an accumulation of scientific facts has resulted that we have today a complete knowledge of the essential truths of malarial disease, including its cause, manner of infection and conveyance, the life-history of the malaria parasite, the clinical course and pathology of the disease and absolute methods of diagnosis, prevention and cure. For the accomplishment of this great work credit is due many workers, but it will not be invidious to mention a few of the leaders of thought and action, French, English, Italian, German and American, along the paths of investigation. Among the most conspicuous of these men are Laveran, Manson, Ross, Bignami, Celli, Marchiafava, Koch, Plehn, Osler, Dock, Thayer and Mac Callum.

Geographically, malarial disease occurs in almost all parts of

the world, being entirely unknown only in the coldest portions and in the waterless deserts. Limits of lattitude in which it occurs are sometimes given as 64° N. and 20° S. for the Eastern hemisphere and 55° N. and 30° S. for the Western hemisphere, but these statements will probably be found to require revision. Its distribution corresponds with that of Anophelina mosquitos and wherever these insects and man are found together the disease may occur. Remembering the ability of the mosquito to hibernate in winter, we can understand how they are able to exist in all countries where mild weather occurs, even briefly, at some time of the year, the adult hibernating insects living from warm season to warm season even though the larvæ perish from freezing. With the advent of warm weather the female mosquito, having remained pregnant in the hibernating stage, lays her eggs. It is in this manner that the species is perpetuated in cold countries.

Malarial disease is most prevalent in moist tropical countries, however, and most pernicious in the East and West Indies, South America, India and tropical Africa and is therefore generally considered a tropical disease, although it is truly cosmopolitan. Strictly speaking, it is an endemic disease although under favorable conditions it may become so prevalent as to permit the use of the term epidemic. Conditions of warmth and moisture favor the breeding of mosquitos and consequently the prevalence of malarial disease. Some authorities have stated that malaria parasites will not develop in the mosquito at low temperatures and have placed the sustained average temperature required at 60° F. Continued observation alone will verify or overthrow this dictum. In Climate and Health in Warm Countries (p. 73), Giles states that: "For the maintenance of malarial fever the co-existence of three animal organisms is essential, viz., of man, the mosquito and the malarial protozoon; and it is obvious that even the temporary banishment of either of the three from any given locality will necessarily put an end to all possibility of the occurrence of fever; for man can be infected only by the mosquito and the mosquito by man, and the presence of both of the others is necessary for the maintenance of the species for the parasite." The absence

of water in the desert explains the absence of mosquitos and malaria. In the Sahara the disease occurs only in the oases. Altitude, drainage, rainfall, heat and moisture affect the prevalence of malaria directly as they influence the breeding of Anophelina mosquitos. The importation of malaria-infected individuals into localities where anopheles mosquitos abound or the importation of infected anopheles mosquitos into a populated locality furnish the conditions for the appearance of the disease in communities where it has not been known, and these occurrences frequently transpire.

Malarial outbreaks at sea have been reported on more than one occasion and while the diagnoses in such instances are rarely microscopic, and therefore open to some question, such occurrences can be readily understood and explained. Infected mosquitos may come aboard a ship in port and bite members of the crew or passengers, in which event we may reasonably expect the disease to develop at sea in due time. Likewise, mosquitos may appear in midocean, apparently from the sky. I have seen this occur in Mid-Pacific, two or three weeks after leaving port. Upon investigation I found that the larvæ were hatched in the small accumulations of rain water in the life boats hanging at the davits, or in sagging portions of their canvas covers, the eggs probably being deposited while the ship was at her docks in port. With a few malarial patients on board, infection of other passengers might easily occur, providing the insects were of the proper variety and the voyage sufficiently long. Another matter with a direct bearing upon the geographical distribution of malarial disease is the transference of mosquitos in railway cars. In 1899, on two or more occasions when detailed to transfer sick soldiers (mostly malarial cases) from the interior of Cuba to the hospital ship in Havana harbor, I was obliged to take a returning train leaving Christina Station in Havana shortly before daylight. Upon each occasion the mosquitos within the cars were almost intolerable for the first hour of the journey. As daylight appeared, however, they sought the walls and ceilings and darker places. Without doubt hundreds of mosquitos were daily carried to the

terminus of the road at Pinar del Rio, one hundred miles distant from Havana. The possibility of malarial disease transference in this manner is too obvious to require further remark. The matters of winds, trees and disturbance of the soil have for many years been believed to exert important influences upon the general and local geography of malarial disease. Many theories of explanation have been built up, exploded and abandoned, but the modern views concerning these influences are simple and satisfactory. These matters have relations to mosquitos, the bearers of malaria parasites, and not directly to the disease itself. Trees, especially low shrubbery, are more apt to harbor mosquitos during the day than they are to prevent them, although in the case of high winds when the insects might be blown from swamps into houses they may act as temporary barriers, after the manner of window screens. Mosquitos seek shelter in winds and probably are rarely blown any great distance.

During a strong breeze they will cling to any friendly shelter, low bushes, trees, close foliage generally and the leeward side of houses. As the breezes subside they take flight and it is conceivable that they may occasionally be carried some distance by the gentler breezes. It is now generally conceded that these insects cannot fly far and they do not, as a rule, rise to any height. This last fact explains the comparative salubrity of sleeping apartments in the upper stories of buildings. By their effect upon drainage of the soil, trees may, perhaps, favorably influence the prevalence of malaria-bearing mosquitos. Certain varieties of trees are said to be so noxious to these insects that they are never found in their immediate vicinity even though the breeding accommodations are first class. The blue gum tree—Eucalyptus globulus—enjoys this reputation in certain sections of California. The explanation of the increased prevalence of malaria during times of soil excavation, lies in the creation of numerous hollows and depressions where water accumulates and mosquitos are bred. It should be remembered in this connection that a very small puddle, containing less than a cupful of water, may breed mosquitos by the hundreds.

Etiology. The causative organism of malarial disease has

already been repeatedly mentioned and we have described in the introduction the mosquito which disseminates it. We will next discuss the parasite itself, briefly sketching its life-history in its two phases, the human phase and the mosquito phase. At the outset it will be wise to remember that future investigators may develop the facts of still other phases of existence for the malaria parasite and that they may even demonstrate other methods of human infection besides that which is now believed to be the only one. While there appears to be no definite indication or promise of such developments, so great an authority as Sir Patrick Manson expressed himself at the International Congress of Hygiene and Demography, held in Brussels in Sept. 1903, as believing that some causative factor besides the mosquito, as yet unknown, may play a part in the etiology of malaria. (Report of Major W. D. McCaw, Unites States Army, delegate to the Congress. Surgeon-General's Report for 1904, p. 117.)

While, therefore, we may not speak with absolute finality in the matter, for our purposes we may safely disregard unsupported predictions of such developments. If they occur they will constitute additional knowledge, in no way weakening the facts of which we are now apprised. The *Hemameba Malariæ* is a protozoal parasite belonging to the Sporozoa and the subdivision Hemosporidia. It is parasitic in its entire existence, requiring as hosts a warm-blooded animal (man) and an insect (the mosquito). Evidence pointing to any other warm-blooded host than man is entirely lacking for Hemameba Malariæ, although closely allied blood parasites infest monkeys, birds and bats.

In its human cycle the parasite reproduces itself asexually by sporulation, i.e., by breaking up into numerous young forms or spores. Each spore or young form enters a red blood cell, develops within it at the cell's expense, and again breaks into spores. This constitutes the asexual or human cycle of the malaria parasite and the parasites so developed are called sporocytes. Certain of the spores do not reproduce themselves by division, however, but assume the sexual form. These individual parasites are called gametocytes and do not reproduce themselves so long as

they remain within the human host; but if they are sucked into the stomach of the anopheles mosquito they become sexually active. Certain of the gametocytes develop flagellate forms (males), the flagellum separating from the organism and penetrating another non-flagellate gametocyte (the female). The fertilized female swells and forms a cyst and divides into several masses which rupture, each giving birth to an enormous number of small thread-like bodies. These bodies are called sporozoites and are incapable of further development outside of the human body. These sporozoites which have been developed within the stomach of the mosquito now find their way into the salivary glands, where the venom of the insect is elaborated, and are finally introduced into the human body by the mosquito's bite. Again within the human body, these sporozoites become sporocytes, entering the red blood cells, and begin anew the asexual cycle. This in brief is the life-history of Hemameba Malariæ. The asexual (sporocyte) cycle is readily studied in human blood under the microscope but the changes of the gametocyte, occurring chiefly outside of the human body, are not as readily studied, mosquito dissection being necessary.

Certain initial changes (exflagellation), of gametocytes may be seen in blood which has been altered by exposure to air and by a slight admixture of water. Indeed, exflagellation may be produced almost at will in specimens, by exposing the shed drop of blood to the air and breathing upon the glass slide before placing the cover-glass upon it. It is not necessary, however, for the busy medical man to follow the various changes in the gametocyte in the mosquito. For diagnostic purposes he deals only with the sporocyte parasite, as found in circulating human blood. The student desirous of pursuing the mosquito phase further will find Daniels' Laboratory Studies in Tropical Medicine of great assistance.

There are at least four varieties of malaria parasites, each one associated with a peculiar variety of fever, but all that has been said concerning the life cycle of the parasites thus far, applies with equal truth to all of the varieties. It cannot be positively

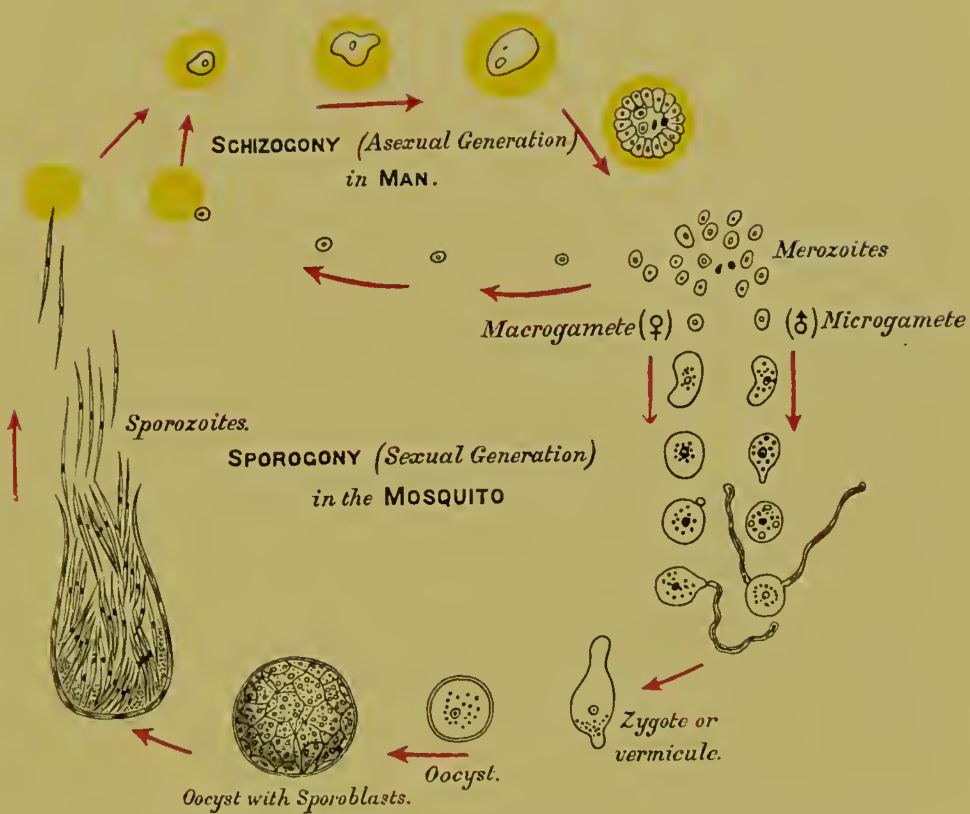


Fig. 43.—Diagram illustrating the human and mosquito cycles of existence of the malaria parasite. (From Martin's General Pathology.)

The term "schizogony" as used in the diagram corresponds with the expression "sporocyte cycle or phase" used by the author in the text; and the term "sporogony" as used in the diagram corresponds with the author's expression "sporozoite cycle or phase."

stated that these varieties constitute distinct species but they are constant in their evolutions and morphology and all are pathogenic. These varieties differ chiefly in the length of their life cycles in the sporocyte phase (the human phase), and in their malignancy. They may be classified according to malignancy and according to the duration of their human evolution cycles.

For purposes of description we will use the classification according to the length of the life cycle. Malaria parasites complete the sporocyte (asexual) cycles in human blood in twenty-four, forty-eight and seventy-two hours (approximately), and are accordingly termed quotidian, tertian and quartan parasites. It should be remembered that this classification is a provisional one, some observers contending that there are but two varieties according to the length of cycles, tertian (forty-eight hours) and quartan (seventy-two hours). There seems to be abundant data, however, to warrant the recognition of the quotidian (twenty-four hours) parasite. In the United States, Craig has studied the malignant quotidian parasite extensively, and strongly asserts its individuality, verifying the contention of the Italian observers who originally described the variety.

The *Quotidian Parasite* is a small organism, associated with malignant fever, which completes its human cycle in approximately twenty-four hours and at full development occupies less than one-half the red corpuscle in which it grows. Two forms are recognized, one of which accumulates pigment, the other does not; they may be found associated in the same individual.

The number of spores into which it divides is from six to ten but sporulation is observed but rarely in peripheral blood. The young parasite has decided ameboid movement and usually develops a ring form. The gametocyte of this parasite is crescent shaped. The fever caused by quotidian parasites is malignant and, fortunately, rather rare. It may be distinctly intermittent or continued. In infection with a single group the paroxysms will be quotidian and the fever distinctly intermittent. If multiple groups are present continued fever will be observed.

There is no benign variety of the quotidian parasite, it being

invariably associated with grave fever or with afebrile expressions such as anemia and cachexia.

Tertian parasites of malarial disease are of two kinds, their one common characteristic being a life cycle of approximately forty-eight hours. There are marked differences in their morphology and pathogenic properties. We will refer to these varieties as the benign tertian and the malignant tertian, the latter variety frequently being spoken of as the *subtertian* or the *estivo-autumnal* tertian. The term malignant seems to be the preferable one.

The Malignant Tertian parasite is less constant in its cycle than the benign tertian, but approximates forty-eight hours. In common with the malignant quotidian parasite, just described, it is rarely observed in the pigmented, sporulating or presporulating stages in the peripheral blood. Sporulation takes place in the recesses of the spleen and other internal organs and in the bone marrow also. The parasite forms from ten to twelve spores and at full growth occupies from one-half to two-thirds of the corpuscle. In its sporocyte stage (human cycle) it resembles the common benign tertian in form, but in its early gametocyte stage assumes the crescent form. This is likewise true of the other malignant variety of malaria parasites, the quotidian, but there are slight differences in form in the crescents of quotidian and tertian malignant parasites. The malignant tertian has an important distinguishing quality in its resistance to quinine, the benign tertian usually disappearing more promptly, and under smaller doses of this drug, than the malignant tertian. The pigment arrangement in the malignant tertian is in fine black granules which early assume a mass formation. An effect of this parasite upon the red blood cell containing it is usually a change in color, the corpuscle assuming a "brassy" hue and later becoming somewhat decolorized. The red blood cell is not ordinarily enlarged and may be shrunken. The fever caused by a single group of malignant tertian (subtertian) parasites is usually remittent but may be intermittent. Multiple groups cause continued fever.

The Benign Tertian parasite is at least a third larger than the malignant one; its asexual cycle is more constant, being about forty-eight hours long. The entire sporocyte stage may be observed in the peripheral blood and the gametocyte form is that of a sphere and not crescentic. Its effect upon the red corpuscle differs from that of the malignant variety in that the cell is never shrunken but almost invariably swollen, sometimes to nearly twice its normal size. The corpuscle is decolorized, often completely, and the "brassy" color is absent. The pigment formed is yellowish brown and finely granular. The spores vary from fifteen to twenty-five in number. The fever caused by a single group of benign tertian parasites is distinctly intermittent, paroxysms occurring every forty-eight hours. If two groups are present the paroxysms may occur every day, the two groups sporulating upon alternate days.

The Quartan Parasite is a benign parasite with a cycle of seventy-two hours for its asexual (human) stage. It is the most constant of the malaria parasites in the matter of regularity of sporulation and segmentation, the spores arranging themselves before segmentation in a manner suggesting the petals of a daisy. They number from eight to twelve. The ameboid movement of the quartan parasite is sluggish and ceases early, about the time pigment appears. The pigment is black and occurs in coarse granules. The color of the red cell is but slightly changed but may be a shade darker than the normal. The red cell is not swollen, as in benign tertian infection, and there may even be slight shrinking. The gamectocyte is spherical, like that of the benign tertian but smaller. The fever caused by the quartan parasite is distinctly intermittent, paroxysms occurring every seventy-two hours if the infection is with a single group. Three groups of quartan parasites might produce quotidian fever.

The morphology of malaria parasites will be further considered in the section upon laboratory detection at the close of this chapter. It should be borne in mind that afebrile manifestations, more or less periodic, occur in infections of all the parasites described, but particularly in the cases of the malignant varieties.

The following tabulation will assist the student in remembering the differences of morphology in the several varieties of malaria parasites.

VARIETY OF PARASITE.	Length of human cycle.	Number of spores.	Ameboid Motility.	Changes in red bloodcell.	Pigment.	Form of Gametocyte.	Sporulates.
Benign Tertian.	48 hours	15 to 25	Very active	Swells and becomes decolorized	Finely granular and brown	Spherical	In general circulation including peripheral blood
Malignant Tertian, (estivo-autumnal Tertian or Sub-tertian.)	48 hours (about)	10 to 12	Active	"Brassy" color corpuscle shrinks	Fine black, forms masses	Crescent	In internal organs
Benign Quartan.	72 hours	8 to 18 arrange in "daisy" form	Sluggish movement ceases early	Slightly darker than normal and contracted	Coarse black granules	Spherical	In general circulation including peripheral blood
Malignant Quotidian, (Estivo-autumnal Quotidian.)	24 hours (about)	6 to 10 (small)	Decided	"Brassy" color corpuscle may shrink	Fine black	Crescent	In internal organs

As has already been pointed out the seasonal prevalence of malarial disease is determined by the prevalence of anopheles mosquitos and in tropic countries this prevalence is influenced by the rainfall and the consequent abundance of puddles of water which serve as breeding places. My observations in Cuba and the Philippine Islands convinced me that these were the real determining factors in the prevalence of tropic malaria and that, other things being equal, the increase or diminution of standing water was the real index of the prevalence of new malaria cases. The table on page 247 shows the seasonal prevalence of malarial fevers in Pinar del Rio, Cuba, during the year 1899 and was prepared by me from the official sick report of the military post maintained there, in which I was a resident. The fluctuating population is indicated by the broken line,——. The dotted line .... indicates the number of cases of sickness from all causes and the black straight line indicates the number of cases of malarial fever.

In view of the similarity of conditions in Cuba and Panama it should be a fair guide as to the seasonal prevalence of malaria in the latter country under normal conditions; not taking into account the disturbance of the soil and the consequent increase in the number of puddles where mosquitos might breed, or the increased facilities for protection from mosquitos which the sanitarians in charge of the Isthmian canal digging will provide.

In the accompanying table it will be seen that the population of the post varied from 1768 in February to 479 in December. The monthly number of cases of sickness from all causes was highest in August when 600 were recorded in a population of 1197, but the largest absolute number of cases of malarial fever, 443, occurred in September when the population was only 883, something more than 50 percent. of the mean strength of the post suffering. During my experience in the Philippines I never saw this percentage attained or approached. (See table p. 247.)

Concerning immunity against malarial infection, there has always been and there still exists much contradictory testimony. In recent years Koch has given the matter careful consideration in connection with his studies of malaria in Africa and he considers the immunity of the natives to be due to recovery from malaria without quinine. It has been supposed that Malays, Mongolians and Negroes possess, naturally, a degree of immunity against infection and that in the case of the Negro this immunity is of considerable degree. At best this so-called immunity must be described as a lessened predisposition. The thickness and offensive odors of the Negro's skin probably repel the mosquito to a certain extent but Negroes *do* suffer from malarial infection. Scheube states that the negroes of German East Africa who dwell in a certain mountainous district acquire malignant infections when they go to certain coast points and that when they recover from these malignant attacks they possess immunity. This immunity is enjoyed by the permanent dwellers in these coast localities and descends through generations. It is lost, however, if the individuals remove to other climates. Personally, I am inclined to look upon such immunity as a condition of latency

and believe that these infections persist for years. In the Philippines I embraced the opportunity to examine the blood of native military prisoners who were supposed to be in health and the number of individuals showing malaria parasites in the blood was

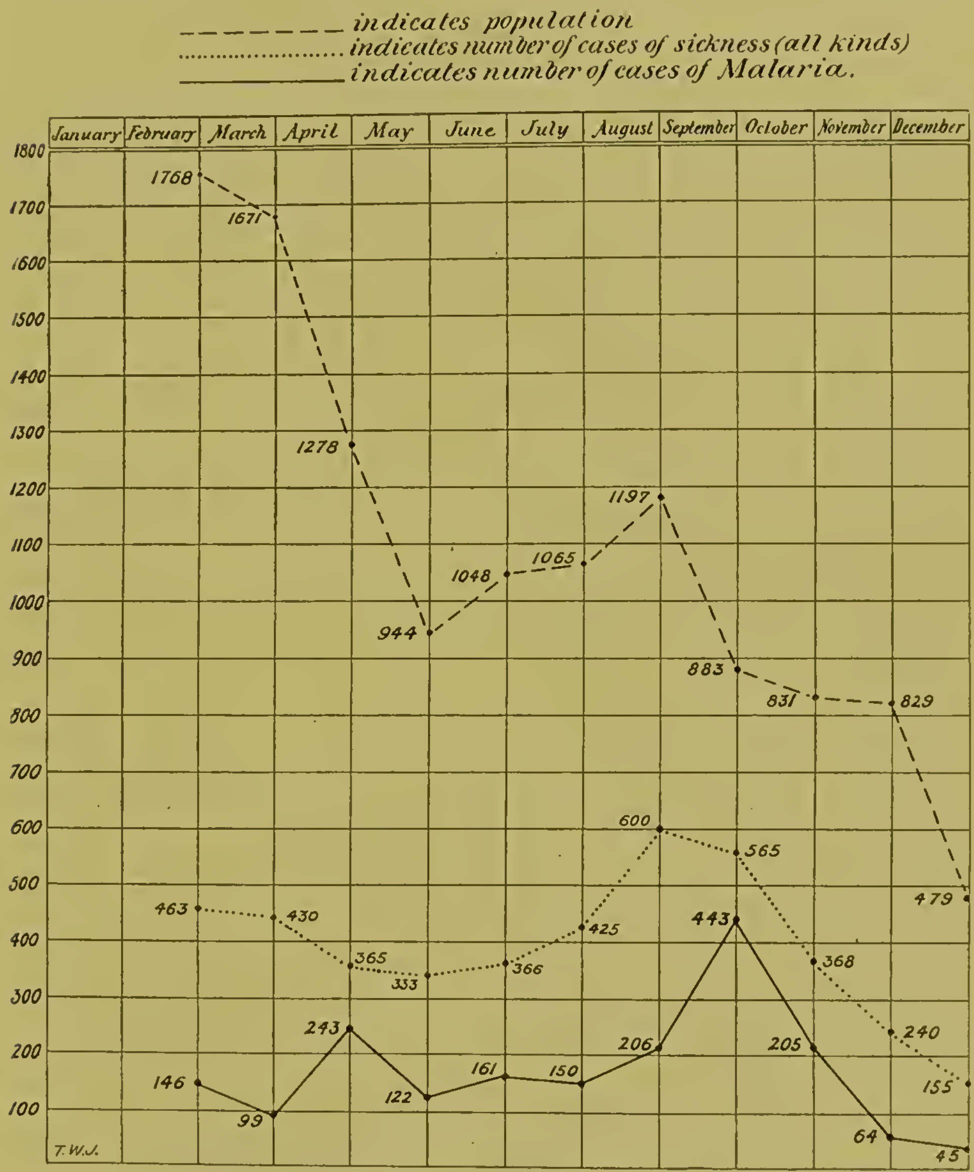


Fig. 44.—Table showing seasonal prevalence of malarial fevers in Pinar del Rio, Cuba.

surprising. It was also observed that when these prisoners were put to work many of them promptly developed fever and some few died with pernicious symptoms.

Unusual exertion, such as road making and other public works, under which the Americans maintained fair health, seemed to arouse these latent parasites to pernicious activity in the Malays. Other recent observations in tropic countries indicate that the native population suffers from latent malarial infection to a degree not hitherto suspected. Having observed many cases of latent malarial infection in Americans, both in the tropics and after returning therefrom, I am convinced that racial immunity is a less important consideration than latency of infection. In the latter condition unusual stress of any kind, which lowers the vitality of the individual, may cause latent parasites to multiply to such an extent in the blood of the human host as to overwhelm the protective forces of the organism. In this event we have the manifestations of acute malaria. It has been asserted that the fetus may acquire malarial disease through the blood of the infected mother and that the child may be born with a malarial infection. Individual predisposition will be increased by occupation and insalubrious surroundings (mosquito-infested houses) or enfeeblement from any cause. Age and sex do not protect to any appreciable degree, except as they may lessen exposure to mosquitos.

The *invasion period* of malarial disease is variously given by various writers upon the subject. Experimental infections, by injecting blood from malarial subjects into healthy individuals, have been repeatedly made but are unsatisfactory and seem to vary according to the amount of blood injected. Scheube states that from ten to fourteen days may be taken as the average period of incubation (for all varieties). Thayer in his "Lectures upon Malarial Fevers," p. 100, gives the following periods for the different parasites. (Maximum in days.)

Benign Tertian, 12 days. Benign Quartan, 15 days. Malignant (estivo-autumnal), 5 days. The periods given by Thayer were determined in cases of inoculation of malarial blood—from one person to another—and do not take into account the intra-mosquito cycle of the parasite's existence.

The point to be determined is the length of time which elapses

between the instant of inoculation of the sporozoites and the first appearance of paroxysm or fever. It seems not at all unlikely, as contended by a number of observers, that this period is a variable one and that the variation is an extreme one depending on certain ill-understood conditions of the subject of inoculation and the stage and variety of the inoculated parasites.

The following eighteen cases, reported by me in "American Medicine," July 9, 1904, seem to give force to the proposition that, under the same conditions, the period of incubation for a number of individuals inoculated by mosquitos with the same malarial parasites, at approximately the same time, varies but slightly.

The parasite with which we have to deal in this instance is the tertian variety of the estivo-autumnal family.

The period of incubation for this parasite, the malignant tertian, as given by various authors, varies from four to twenty days.

Craig, says, "that the most satisfactory datum we possess is that given by Marchiafava and Bignami," and he quotes three cases cited by them wherein there existed practically no opportunity for error, in which the incubation period was from nine to ten days.

The difficulties attendant upon reaching accurate conclusions in this matter, in all cases except experimental inoculation cases, i.e., in all cases where inoculation occurs naturally by medium of the mosquito, are apparent. Craig also points out that the observations of natural inoculations are the only ones of value in determining the incubation period.

Upon April 11, 1902, at 7:00 A. M. forty-five men of Troop A, Sixth United States Cavalry, left the station of Naic, in Cavite Province, Philippine Islands, to take part in certain operations in the field in the vicinity of Gonzalez Mountain. They were absent from their station eight days and seven nights. Two of these days were spent on the march and one night, that of April 11th, was spent at the town of Silang, en route. The nights of April 12, 13, 14, 15, 16 and 17 were spent in camp under shelter tents. Mosquito canopies were used at the home station

(Naic) and had been used by these men up to the time of their departure but were not taken into the field. The troops returned to their home station upon the evening of April 18th, the men apparently in good condition. During the time in the field the health of the command was reported excellent, but one case of fever, a recurrence of a chronic infection lasting but a day, being reported. During the same period there was but one admission for malarial fever from the men of the troop left behind in the garrison.

The camp site, occupied for six days and nights, had not previously been occupied by American troops and there were no houses in the vicinity.

There was one outpost a short distance from the camp and a guard, consisting of a noncommissioned officer and three men, was maintained there from the 13th to the 17th of April, inclusive. As neither Surgeon nor Hospital Corps attendant accompanied this expedition my information concerning the camp and its surroundings was obtained from members of the expedition.

During the week following the return of the expedition to the garrison no cases of malarial fever were admitted from Troop A, Sixth Cavalry.

Within forty-eight hours from the night of April 25th, eighteen men from the returned expedition were stricken with malarial fever and fifteen were admitted to the hospital. During the same period there were no admissions from the detachment which had remained in the garrison.

The blood of each case was examined microscopically before quinine administration was begun and estivo-autumnal parasites (malignant tertian organisms) were found in each specimen, in most cases in great profusion. The parasites were unmistakably of the same variety. The fever in each case was sharp and remittent in character and lasted from two to six days. The fever curve (except as obscured by quinine administration) and the clinical manifestations were those of malignant tertian fever. There were no spontaneous cures, rather massive doses of quinine being required.

In the present group of eighteen cases the following facts bearing upon the incubation period are known: The date upon which the men went into camp without mosquito canopies, and consequently the first date upon which general inoculation might occur, was April 12th.

The time of the outbreak of the epidemic was the forty-eight hours from the night of April 25th to April 27th, inclusive.

Systematic blood examinations in all cases of malarial disease at the post of Naic had been made and recorded. A review of this record for the preceding six months showed that only three of the eighteen cases had suffered from malarial disease in the past half year and but one case within the month preceding this outbreak. Curiously, in this case the previous attack was a clear case of benign tertian infection and in the present attack both benign tertian and estivo-autumnal tertian organisms were present in the blood, i.e., a double infection. Clearly the present attack was a fresh infection with the malignant tertian (estivo-autumnal) organism, as were the other seventeen cases.

If we take the twenty-four hours ending upon the evening of April 14th as the first day of exposure and assume that all of these cases were inoculated within twenty-four hours, we find that there was an incubation period of twelve days for those cases which were stricken on the night of April 25th, and of thirteen days and fourteen days respectively for those stricken on the nights of April 26th and April 27th.

These are somewhat longer periods than in the three cases cited by Marchiafavi and Bignami referred to above, and it is probably not fair to assume that these eighteen men were all inoculated within twenty-four hours.

Indeed the facts seem to indicate that this did not occur.

Careful inquiry of the men affected as to where the mosquitos were most troublesome elicited an expression quite unanimous, to the effect that they were much worse at the outpost mentioned above.

The records show that forty percent. of the expedition were infected and that of those men who did outpost duty sixty-five

percent. were infected. We, also, find that about seventy-two percent. of the whole number of sick were those men who did outpost duty.

Or, to state the case otherwise, of the men who did no outpost duty about eighty-two percent. escaped infection, while of those who performed outpost duty thirty-five percent. only escaped.

These facts are too significant to permit us to escape the conclusion that the victims were, in most cases, infected while upon outpost duty. A few of the men performed more than one tour of guard duty at the outpost during the five days it was maintained and for this reason and other circumstances relating to the relief of the guard, rotation, etc., it is difficult to carry the investigation further.

It seems fair, however, to take the midpoint of the 120 hours during which this outpost was maintained and the midpoint of the forty-eight hours during which the men were admitted to the hospital sick, as reckoning points to determine an average incubation period. This done we ascertain the average to be twelve days. If, now, however, we allow each man twenty-four hours immediately preceding admission to the hospital as a portion of the period of sickness we reduce the invasion period to eleven days and if we make this allowance forty-eight hours (the period required for the complete cycle of the causative parasites in these cases) we reduce the incubation or invasion period to ten days, which closely corresponds to the observations of the Italians named.

It is certainly fair to make some allowance of this kind, bearing in mind that the patient does not ordinarily seek the hospital until too ill to continue his duties.

In view of the above stated facts it is believed that the following is an accurate statement of the case: In an epidemic of eighteen cases of estivo-autumnal fever (of the malignant tertian variety) which occurred in Troop A, Sixth United States Cavalry, in the Philippine Islands in April, 1902, *the invasion or incubation period was between ten and eleven days.*

It has seemed futile to attempt to locate the original human

source of infection in this epidemic. Should we look for it in a latent or passive infection existing in some member of the expedition, we are confronted with the fact that the parasite undergoes an intramosquito (a reproductive) cycle preceding the formation of sporozoites in which form the parasites are inoculated, and that this intramosquito cycle occupies a period of about ten days, according to Manson, Ross and the Italian observers. It would be impossible to harmonize the facts and dates of this exposure and epidemic with such an hypothesis and we are therefore led to conclude that the inoculating mosquitos in this epidemic obtained the malarial parasites from some other human source, probably from native Filipinos who had previously been in the vicinity, it being a fact, well known and proven, that the natives suffer extensively from malarial disease, both in its active and latent forms.

Closely related to the subject of etiology is that of *prophylaxis.* We cannot by any possibility escape the conclusion that the prophylaxis of malaria means the destruction of anopheles mosquitos and protection from their bites. We have considered their destruction in the preceding pages and we may now take up the alternative matter of protection from their bites.

Given a case of malarial fever we are bound to protect the individual and the community or household in which the patient lives. We may make war upon the insects or their breeding places in and about the house or premises and we may exclude mosquitos by screened doors and windows, but of the greatest importance is the isolation and screening of the patient, in order that the mosquitos themselves may not become infected from him and convey the parasites to others. Nor should we lose sight of the fact that a patient convalescing from malarial fever may be reinfected by being bitten by mosquitos which have fed upon *his own* blood in previous weeks, during the period when the blood was laden with parasites. I am satisfied that this method of self-infection is quite common. There is no lack of evidence as to the acquiring of malarial disease in hospitals and barracks. In 1900, in Cuba, patients admitted to the hospitals for entirely distinct diseases developed malarial fever in our wards, having

been there longer than the maximum incubation period. They were undoubtedly bitten by mosquitos which had fed upon the blood of malarial cases in the same hospital ward, or in adjacent wards, and *after* their admission to the hospital. This occurred within my own experience repeatedly. The use of the mosquito canopy was not as rigidly insisted upon then as now and isolation was practically ignored. In the light of what we now know positively, such omissions would be culpable negligence today.

Wire screen material is preferable to the ordinary cotton mosquito netting as it is far more durable, retains its position and is less liable to accident. If the cotton netting canopy is used over the bed it should be large and should not touch the bed or mattress at any points nor be tucked under the mattress. If permitted to touch the bed the patient's body may come into contact with the canopy during sleep and mosquitos may feed upon the patient through the netting. The lower border of the canopy skirt should be kept close to the floor by weights, or attached to stiff strips of wood or wire which should rest on the floor. A folding frame or cage, covered with wire netting and sufficiently large to completely surround the bed and leave a space for standing room between the bed and the screen, will be found superior to the cotton canopy net and in the end will be quite as economical, as it will rarely require renewing and if made of bronze or copper netting will not rust. Cotton canopies require frequent washing and rapidly become worthless. Obviously, mosquito canopies over beds do not *absolutely* protect the persons who use them from infection, as individuals in health rarely spend more than a third of the time in bed and although nearly all varieties of mosquitos are more or less nocturnal in their biting habits, none are strictly so and there is a large chance that one will be bitten at least once or twice during the daylight hours.

The Prophylactic Use of Drugs in malarial disease has long been a subject of discussion. Many drugs have been recommended as capable of developing immunity in man, but perhaps not more than half a dozen have had serious supporters. Of these the most popular are, quinine, arsenic, and iron, named in the

order of their medical popularity. Each drug has had strong advocacy. The military medical officers of countries with tropic provinces have, perhaps, the best opportunities to form accurate judgments in the matter, and their opinions are therefore of great value. Until recent years the United States could not claim the right to an opinion founded upon extended tropical experience, but during the past seven years she has acquired this right. Armies, living under tropic conditions, especially during active field service when men are not housed and are particularly exposed to mosquitos, offer the best opportunities for observing the prophylactic use of drugs. British, French, German, Italian, and I think I may add American, military observers give first place to quinine, although there is much difference of opinion as to the best manner in which to use it. Arsenic and iron both have some adherents. An experience with arsenic in Cuba, in 1899, convinced me of its uselessness as a prophylactic drug. During this year, at the instance of his medical advisers, an order was issued by the general in command to administer arsenic to all soldiers, in the hope that the incidence of malarial fevers would thus be reduced. Accordingly, during the spring months the men in at least two large posts received Fowler's solution in two and three minim doses three times daily. It is only necessary to refer to the graphic chart on page 247, showing the seasonal prevalence of malaria, to note its utter uselessness in preventing malaria infections, in at least one of these posts. This chart shows the prevalence of malarial disease in the very troops and companies subjected to the arsenic experimentation. The routine administration of arsenic in the manner described is not, in my opinion, a justifiable experiment and certain individuals with idiosyncrasies are bound to develop disagreeable effects. On the other hand, most authorities agree that quinine used as a prophylactic will reduce malarial morbidity in bodies of troops or workmen, very decidedly. My individual experience coincides with this belief although I have had no experience in the wholesale or routine administration of quinine to soldiers. Old campaigners, however, recognize the protection afforded by its use and often apply for it to the surgeon when about

to start on an expedition involving exposure. Koch and his assistants in Africa, and Grassi, in Italy, claim to have practically abolished malaria in certain small communities by administering quinine to all malarial subjects regardless of color or race. The German method of administering quinine for prophylaxis is to give ½ to 1 gram (7½ to 15 grains) every three, five or eight days, preferably at night on account of the tinnitus produced. The method of the British and French is to give the drug in three to five grain doses daily. Manson and Duncan advocate this method while Treube, Koch, and others, give preference to the former method, claiming for it that the chance of destroying malaria parasites which may have invaded the body is greater with the larger dose, even though given less frequently. The disagreeable and injurious effects of quinine used habitually seem to strengthen the claims of the Germans. The digestive and nervous systems receive the brunt of the drug's effects, although it is not unreasonable to expect damage to the kidneys if the use of quinine is continued for years. In common with many other drugs, quinine, continually and habitually used, seems to lose something of its potency. This is by no means as true of quinine as of other alkaloids, however.

There is some reason to believe that methylene blue, used as a prophylactic in the same manner as quinine, has virtues similar to the older drug, but the evidence is still inconclusive. The therapeutic values of iron and arsenic depend, in my opinion, solely upon their restorative and reproductive action upon the red blood corpuscles and not to any destructive action upon the protoplasm of parasites.

After all, the most promising measure of prophylaxis that can be advocated is a general campaign of education for both medical men and the laity. The widespread lack of understanding, on the part of medical men, of the manner in which malaria is conveyed, of the part the mosquito plays in its conveyance, and of the practical possibility of abolishing malaria from communities, is at present the greatest obstacle to substantial achievement. This education of the medical profession is under way but has not reached the outer boundaries of the

profession by any means; moreover, it is an absolutely essential preliminary to the education of the lay public. I am inclined to coincide with the conclusions of Celli and Casagrandi that, "While the problem of destroying mosquitos is experimently solvable, it will practically be so only when economic interest desires it." And this involves the education of the public in the mosquito causation of malaria. Manson correctly states that "Sanitary measures can rarely be carried out effectually without the co-operation of those who are interested or benefited, and this co-operation cannot be secured unless the rationale of their operation is understood," therefore, those responsible for the public health in malarial districts should by one means or another indoctrinate the people in the mosquito-malaria theory.

Pathology and Diagnosis. The pathological changes in malarial disease are both macroscopic and microscopic, and, naturally, are widely distributed throughout the entire body in all tissues and organs supplied with blood, in which the parasite lives and works its destruction. Where the blood channels are narrowest, namely, in the capillaries, and in the most vascular organs, the destructive changes are greatest. If we study the blood as a tissue we will find that profound changes are wrought in it by the malaria parasite. These changes include hemolysis and a diminution in numbers and hemoglobin value of red corpuscles, an actual diminution in the blood volume (according to Manson), and intravascular pigmentation of two kinds: A black pigment, characteristic and peculiar to malaria, and a yellow pigment, which is also observed in certain other diseases in which hemolysis and the rapid liberation of hemoglobin occurs. Poikilocytosis, or deformity of the red cells, is also commonly observed, and leukopenia is the rule. This general reduction of leucocytes is quite distinctive and is associated with an increase of the large mononuclear white corpuscles, both actual and relative, so that the combination constitutes a rather significant diagnostic symptom; a percentage of large mononuclears above twelve, in combination with relatively increased eosinophiles and a leukopenia, being a strongly suspicious circumstance.

Leucocytosis may occasionally occur and is usually accounted as indicative of grave infection, of complications, or associated disease. The reduction in the number of red corpuscles may reach one-half or one-fourth, or even more, and is in proportion to the number of parasites present.

Megalocytes, microcytes, and pathologic (nucleated) reds, may occur; the changes, in fact, being those of anemia, grave or mild, with the added presence of parasites, living or dead, whole or fragmented, and the two pigments mentioned.

Pigment is also observed in the form of flakes or granules, included in leucocytes and in the endothelial cells of blood vessel walls, while most of the organs of the body exhibit pigmentation chiefly along the course of blood vessels. Pigment may also invade the tissue elements in the spleen and liver. The organs and tissues most apt to show pigmentation are the skin, serous membrane, liver, heart, kidneys, brain, spinal cord, lymphatic glands, lungs, bone marrow, and most frequently, the spleen. In some severe cases, however, the spleen is the only organ showing pigmentation. Pigmented tissues are slaty or chocolate-colored according to anatomic circumstances. True black pigment is absolutely diagnostic of malaria (according to Manson), and is not to be confounded with the intracellular pigment of tissues in malignant melanotic tumors, nor with the pigment-like dot in lymphocytes in normal blood. Extravascular malarial pigment is only found in old cases of malaria.

Taking up the pathologic anatomy of special organs we find that the *heart* is usually dilated, relaxed, and pale, with or without fatty degeneration, and that extensive thrombi are frequent.

The *liver* changes vary according to the acuteness or chronicity of the disease. In acute malaria the organ is large, hyperemic, dark and soft, and apt to be bile stained. The interlobular spaces sometimes present pigmentation in such abundance that it appears as surrounding black zones about the lobes. Intralobular capillaries usually contain great numbers of parasites, which may completely block them. No black pigment is to be found in the hepatic cells, but yellow pigment may be observed.

The hepatic cells may be normal, atrophic, or necrotic, or they may show cloudy swelling or fatty degeneration. In chronic cases the liver is usually in a state of hypertrophic cirrhosis, and much pigmented, with a thickened capsule; and it may show amyloid degeneration.

The *spleen* will generally be found to be enlarged; in recent cases from hyperemia, and in chronic cases from hyperplasia. In acute cases it will be soft, the pulp appearing tarry and difluent, and it may even simulate the appearance of a bag filled with black blood. In chronic cases it will be found hard and firm, and the thickened capsule will be found adherent to related structures. Enlarged spleen is not so universally the rule in tropic malaria as is generally supposed and taught. In some hundreds of cases in the Philippines and in Cuba, examined for this condition, I failed to find it, and, postmortem, the condition of soft difluent spleen with very moderate swelling is common even in chronic cases. The suggested test of the salubrity of a given region by the condition or absence of splenic swelling in its people is fallable in the extreme. In a good many severe cases of malarial fever I have been unable to even palpate the spleen. In Madagascar, Rochard found no splenic enlargement in twenty-two fatal cases of malarial fever examined postmortem (Schuebe, Diseases of Warm Countries, page 153).

The *bone marrow* will be found to be hyperemic, soft, or even semiliquid, and dark. It usually contains an enormous number of parasites within the vessels and even in extravascular situations in the medullary substance.

The *kidneys* are often normal except for pigmentation, but they may show any one of the different varieties of nephritis, early or advanced.

In the *brain*, cortical pigmentation of the cerebrum, either gray or chocolate colored, may be observed. The cerebral vessels may contain many parasites and thrombotic occlusion with hemorrhage may be due to actual plugging of the capillaries by parasites.

The *muscles* may be normal, or may show fatty degeneration.

The *lungs* may be normal, hyperemic, edematous, or pigmented.

The *gastric mucosa* may be normal, hyperemic, or ecchymotic, with more or less necrosis of the superficial layer. The *intestinal mucosa* may occasionally show pigmentation. In a specimen examined at the Medical Museum in Washington, in 1899, from a case of pernicious malarial infection, the following conditions were observed:

"Complete necrosis of the superficial layer of the mucosa and in places the necrosis extends down to the submucosa. The necrotic debris on the surface contains cells which are probably endothelial cells, loaded with melanin, and in addition there is a sprinkling of fine granules whose source cannot be determined, perhaps the result of hemorrhages. Many of the capillaries of the mucosa are literally crowded with malaria parasites. Abundant malarial pigmentation is present in the vessels of a fragment of fatty omental tissue attached to the stomach." (Report, Surgeon-General, United States Army, for 1899, page 295.)

Although most works upon medical practice speak of the **Diagnosis** of malaria as presenting few difficulties, my experience and observation lead me to quite a different conclusion. I am of the opinion that, except in the regularly intermittent fevers, quite the contrary is true, and that few diseases, if any, present greater difficulties to accurate diagnosis by symptoms and physical signs alone. We should, I believe, designate any diagnosis of malaria based solely upon these signs as *approximate* in distinction from one based upon blood study which might be termed *absolute*. Butler (Diagnostics of Internal Medicine, p. 708) states that: "There is no doubt that the term 'malaria' has been used and is used to cover a multitude of diagnostic sins, an evasion which perhaps is pardonable in view of the technical skill and experience which is requisite to give value to a *negative* result of a blood examination for the plasmodium. It is a good practical rule to *suspect* malaria but to be extremely chary in making a positive diagnosis unless the symptoms are absolutely typical and perhaps not even then without the finding of the hematozoon." (Italics mine.—T. W. J.)

There is but one absolute and accurate method of diagnosis, viz., the microscopic examination of a specimen of the patient's blood. All other methods are fraught with elements of error. The microscopic method is exact, accurate and invariable. Even in the cases of estivo-autumnal infection (malignant parasites), where the peripheral blood shows few or no parasites, the presence of pigment and the leucocytic phenomena described, permit diagnosis.

In the benign infections, the regularly intermittent malarial fevers, and in occasional afebrile cases, parasites and pigmentation are always present and are so readily to be found that objections to the microscopic method on the grounds that elaborate technical knowledge is requisite cannot be advanced. Any medical man with a general knowledge of the use of the microscope can acquire, in a short time, with the aid of one of the several excellent works upon diagnosis, the necessary technical skill. A knowledge of the staining of parasites for permanent preparation, although highly desirable, is not essential; very satisfactory results being obtainable with fresh blood films. The methods and technique of examining malarial blood in both fresh and stained preparations, and instructions for distinguishing varieties, will be found in the special section at the close of this chapter and in the differential table on page 245.

The prevalent idea that the previous administration of quinine makes useless a search for the parasites, is not, in my experience, entirely correct. The presence of moribund or fragmented extracellular malarial organisms in the plasma, and of pigment-bearing leucocytes and deformed red corpuscles, is of great value and may be observed for some time after quinine has been administered; and, indeed, a certain number of motile organisms often persist in the blood for a short time after a sufficient amount of the drug has been given to terminate the fever.

The diagnosis of the irregular malarial fevers is rendered less easy than that of the benign fevers by reason of certain facts connected with the life cycles of the estivo-autumnal parasites. As the young parasites increase in size, they, with the red blood cells

which contain them, show a decided disposition to retire from the peripheral circulation. As the young hyaline forms begin to accumulate pigment they become less and less numerous in the peripheral circulation and during the stage immediately preceding sporulation, and during that process, they are but rarely to be found there. On the contrary, they are present in immense numbers in the blood of the spleen during and preceding the sporulating period. While aspiration of the spleen to secure blood specimens is probably justifiable occasionally, it is certainly attended with greater risk than the needle prick for the extraction of a drop of blood from the ear or finger. I have, in a few cases, observed sporulation of the estivo-autumnal parasites in blood obtained from the ear, but it is by no means a common observation. It is owing to this tendency of estivo-autumnal parasites to disappear from the surface circulation, as they approach sporulation, that there is such difficulty in determining the exact time of their cycles. There is considerable difference of opinion concerning these points, and they are doubtless less constant periods than those of the benign parasites. Those who hold the opinion that there is but one variety of malignant (estivo-autumnal) parasites (and there are more than a few eminent men of this opinion), believe that the cycle is a variable one in point of duration, its length being given as from twenty-four to forty-eight hours. Without entering into a discussion of the belief that there is but a single species of malignant parasites, which view I formerly held, I must state again that the testimony of the Italian observers and of Manson, and the careful studies of Craig in the United States, confirmed by my own experience, have convinced me of the existence of at least two varieties of malignant parasites with fairly marked distinctive characteristics of morphology and evolution. Concerning the febrile expressions of these two varieties of malignant parasites it must be said that they are not usually distinguishable clinically, and in using the terms malignant, or estivo-autumnal, in connection with nonmicroscopic diagnosis no distinction will be made.

However scientific and desirable it may be to make use of the

microscopic method of diagnosis, circumstances very often make it impossible, and we are, therefore, obliged to consider the less accurate manner of diagnosis by physical signs and symptoms, or, approximate diagnosis.

The teaching that fevers which resist quinine are not malarial in origin, even when limited to the intermittent varieties, will not stand the test of experience, as reference to certain original charts in this book, reproduced from actual cases, will prove, and it is, therefore, unsafe to make this unqualified statement. It is, however, the rule that an intermittent fever which does not *respond* to daily doses of twenty or thirty grains of quinine is *probably not* malarial, and I believe that next in value to the microscopic method comes the therapeutic method of diagnosing by quinine. A possible source of error lies in the manner of administration of the drug. In my opinion quinine should, whenever possible, be given in solution or capsules to insure its absorption. I have repeatedly recovered from the stools of patients, quinine tablets of various makes, and gelatine coated pills which were readily compressible and apparently fresh. It is but fair to state that in every such case digestive derangement of some form was present, but it is well known that such derangement is fairly constant in all malarial fevers. Another element of error lies in the use of insufficient doses. The drug should be rapidly pushed to cinchonism, a condition caused in different individuals by widely variable doses.

Few observers have laid much stress upon the possibility of recognizing the youngest forms of the sporocyte phase of the parasite (i.e., immediately following sporulation), but I believe the organism in this stage is more frequently to be recognized, free in the blood plasma, than is generally supposed.

The size of the red blood cells containing a partly grown parasite of either one of the estivo-autumnal varieties is almost invariably smaller than its fellows, while the partly or full grown benign tertian parasite, by far the more common of the two benign families, causes the corpuscle containing it to appear swollen and larger than its fellows. This is a point of differentiation which I deem

of considerable value and more to be relied upon for constancy than the so-called "brassy" color of the corpuscle caused by the invasion of the malignant parasite. This change of color is, however, usually apparent in infections with malignant organisms.

Exflagellation is to be observed in both the benign and the malignant parasites, and is, therefore, of little use in differentiation between them, unless studied in connection with the corresponding gametocytes. The presence of crescents is, of course, indicative solely of the malignant parasite, but these gametocytes do not occur in the early stages of estivo-autumnal fever.

A microscopic evidence of malarial disease not lightly to be esteemed, is the finding of pigment-bearing leucocytes in the blood, Often when the time of the examination is unfavorable for the discovery of the parasite itself, it is possible in this way to make oneself reasonably sure of the presence of parasites in the blood, and, thus assured, perseverance will usually lead to later detection of the organism. Pigment-bearing leucocytes are so rare in all diseases, other than malaria, that their presence may be considered as almost diagnostic. Naturally, this knowledge is of greatest value in the irregular fevers and in the cases of masked infection.

The microscopic and therapeutic methods of diagnosis of intermittent malarial fever are certainly the methods most worthy of consideration. When the microscopic method is not available the therapeutic is most useful. Scientifically the therapeutic diagnosis should rather be a confirmative test, to be used after the microscopic. If made use of first, it invalidates, to a certain extent but not completely, as has been shown before, the microscopic diagnosis.

Exclusive of blood examinations and the response to quinine administration, periodicity of manifestations is the most important sign of malarial disease. This periodicity manifests itself by recurring paroxysms, usually of chill, fever and sweating, in the sequence named, occurring at such times as the particular group of parasites at work ripens and sporulates. As will appear later on, this periodicity is particularly distinctive of infection

with the benign parasites of malaria. Benign malarial infections, usually expressing themselves by intermittent fevers, may simulate, more or less closely, the following diseases:—tuberculosis, pyemia (including liver abscess and concealed collections of pus generally), pyelitis, ulcerative endocarditis, gall stones, and suppurative cholecystitis.

Estivo-autumnal malarial infections (i. e., with malignant parasites) may simulate yellow fever, typhoid fever, dysentery and Asiatic cholera.

The following differential tables may be useful to students. They are neither complete nor infallible, and it should be remembered that malarial infection may occur in the subjects of any of the diseases mentioned, and vice versa. In this event malarial disease must be diagnosed by the microscope, and the complicating disease by its physical signs and symptoms.

Intermittent (Benign) Malarial Fever.	**Tuberculosis.**
The infection is with either tertian or quartan parasites which are demonstrable in peripheral blood.	Physical signs present. Parasites absent from the blood. Melanemia absent. Bacillus tuberculosis present in body and usually demonstrable in sputum. Leucocytes are reduced. Chills, fever and sweating are apt to be quotidian. Quinine does not control.
Chills, fever and sweating occur in regular paroxysms.	**Pyemia.** (Includes liver abscess and concealed pus generally.) Chills, fever and sweating are apt to be irregular. Leucocytosis usually occurs. No malaria parasites or pigment found in the blood. Quinine does not control.
Leukopenia, with a relative increase of large mononuclear white corpuscles, is present. Parasites are present in blood. Melanemia is present.	**Pyelitis.** Pus in the urine. Pain and swelling in lumbar regions. No parasites or pigment in the blood. Quinine does not control the disease. Leucocytosis is usually present. Chills, fever, and sweats, are irregular.

Intermittent (Benign) Malarial Fever.	Ulcerative Endocarditis.
Quinine controls the disease.	Physical signs in chest. Leucocytosis present. Parasites and pigment absent. Quinine does not control disease. Chills, fever and sweats irregular.
Disease conveyed by anopheles mosquitos. Spleen apt to be enlarged.	**Gall Stones or Cholecystitis.** Colic, icterus, local tenderness or swelling are common. Leucocytosis frequent. No parasites nor pigment. Quinine does not control the disease. Chills, fever and sweats irregular.

Table of Differential Diagnosis between Estivo-autumnal Malarial Fever, and Yellow Fever and Typhoid Fever. (For differential diagnosis between Asiatic Cholera, or Dysentery, and Malaria, see chapters on Cholera and Dysentery.)

Estivo-autumnal Malarial Fever.	Yellow Fever.
Infection due to malignant parasites. They may be difficult to find in peripheral blood, but the younger forms are readily found. Melanemia is present. Leucocytes reduced with an increase of large mononuclear leucocytes. Disease conveyed by anopheles mosquitos. Spleen often swollen. Disease ameliorated and eventually cured by quinine.	Jaundice marked. Black vomit may occur. Quinine of no benefit. Prostration profound. Disease conveyed by stegomyia fasciata mosquitos. Malaria parasites and melanemia absent. **Typhoid Fever.** Often hard to distinguish from a continued case of malarial disease, except by microscope. Rose spots and Widal serum reaction probably present. Chills are insignificant. Leucocytes reduced. Melanemia absent. Quinine does not control. Remission of fever is diurnal, occurring in morning. Spleen may be swollen. Abdominal symptoms probably present.

In connection with diagnosis, and preliminary to the discussion of symptoms and treatment, it will be proper to speak of the matter of periodicity of paroxysms in malarial disease.

Clinically, periodic expression is of three varieties: Tertian, most prevalent of all, in which the paroxysm recurs at intervals of forty-eight hours; Quartan, in which the paroxysm recurs at intervals of seventy-two hours; and Quotidian, in which the paroxysm recurs at intervals of twenty-four hours. It is doubtful whether a *benign* quotidian fever ever depends upon a special variety of the parasite, as do the tertian and quartan types.

Quotidian recurrence can be readily and perfectly explained by the fact of infection with several generations, of either tertian or quartan organisms, which sporulate upon successive days, thus giving rise to the twenty-four hour paroxysms. Most observers accept this explanation, and those who maintain that malignant (estivo-autumnal) parasites are all of one variety, viz., the malignant tertian or *subtertian*, also explain quotidian recurrence of paroxysms by the same hypothesis.

Of the common tertian organisms but two sets are required to produce quotidian paroxysms. I have often observed this combination in cases of benign quotidian intermittent fevers. Such manifestations are properly described as double tertian, or *tertiana duplex.* In the Philippine Islands and in Cuba these benign quotidian fevers were frequently observed and they were always found to be due to several families of the common tertian organism sporulating upon successive days. Frequently they changed to pure tertian types and were promptly cured by quinine after the parasites were reduced to single groups.

In the case of the quartan organism three groups of parasites, sporulating upon successive days, would produce quotidian paroxysms, a condition which I have never personally encountered.

It should be borne in mind that continued fever due to multiple infections of benign organisms is theoretically possible, and Thayer has observed one or two such cases. (Lectures on the Malarial Fevers, page 116.) It is certainly a rare manifestation of benign infection, as these organisms show a tendency to arrange themselves in sharply defined groups. It is very common in both varieties of estivo-autumnal infection, however.

In regard to the use of the term remittent, Manson (Tropical

Diseases, p. 57) writers as follows: "Since it has been found that what was designated remittent fever is produced by quartan, tertian and quotidian parasites—the fact of intermittency or remittency being more or less a matter of accident—it has been considered advisable to expunge the term remittent fever as indicative of a distinct species of plasmodium disease. . . . The intermittency or remittency of any given fever depends in great measure on the simultaneousness, or the reverse, of the maturation of the crowd of parasites giving rise to it. If all the parasites present are of nearly the same age, they mature approximately simultaneously and we have an intermittent; if they are of different ages they mature at different times scattered over the twenty-four hours and we have what is known as a remittent."

The possibility of double infection, with two distinct varieties of parasites, one malignant and one benign, is also to be remembered. Such cases are not very rare in districts or communities where both forms of malarial disease prevail. I encountered this combination in a number of instances in the Philippine Islands and at least once in the United States.

The following five charts are those of five cases of estivo-autumnal malarial infection with the malignant tertian (subtertian) parasite, observed during August and September, 1900, at West Point, New York, and reported in the Philadelphia Medical Journal of April 19, 1902. The cases illustrate phases of the disease least understood by the medical public and the diversity of expression of the malignant tertian (subtertian) parasite. Apparently there is a greater prevalence of estivo-autumnal parasites in this community (West Point, N. Y.) than is ordinarily believed to exist in this latitude. Perhaps the most rational explanation of this prevalence is that the tropical parasite has been locally introduced by soldiers returned from Cuba and the Philippine Islands and that the mosquito is responsible for its dissemination.

The difficulty of promptly and permanently curing such infections is illustrated by the persistence of the condition for over two years in Case I. I have personal knowledge of several cases, not included in this report, in which the parasites have undoubt-

edly existed in the blood for five years in spite of treatment, giving rise from time to time to outbreaks of fever, abortive paroxysms or afebrile manifestations; the blood at such times invariably showing the malignant parasites. In the present series

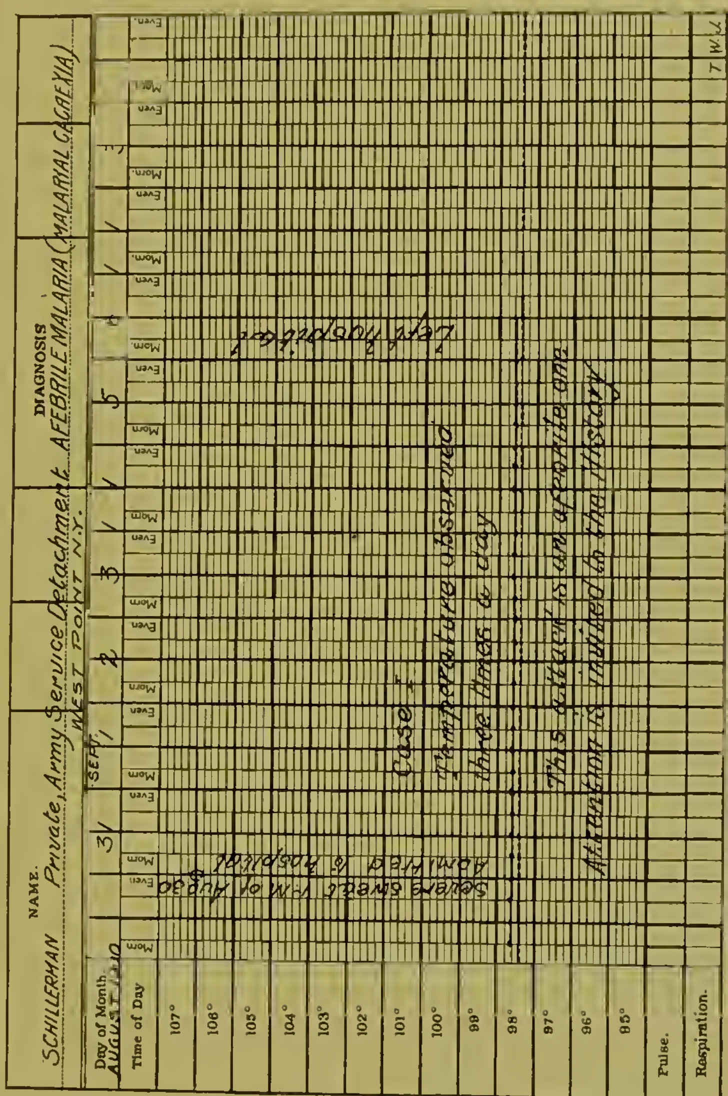


Fig. 45.—Case I.

of cases, studies of both fresh and stained blood specimens were made. The fact that crescents were found in but two of the five cases strengthens my belief that their occurrence should not be depended upon solely in the diagnosis of this condition.

Of the five cases here reported only one originated in Cuba,

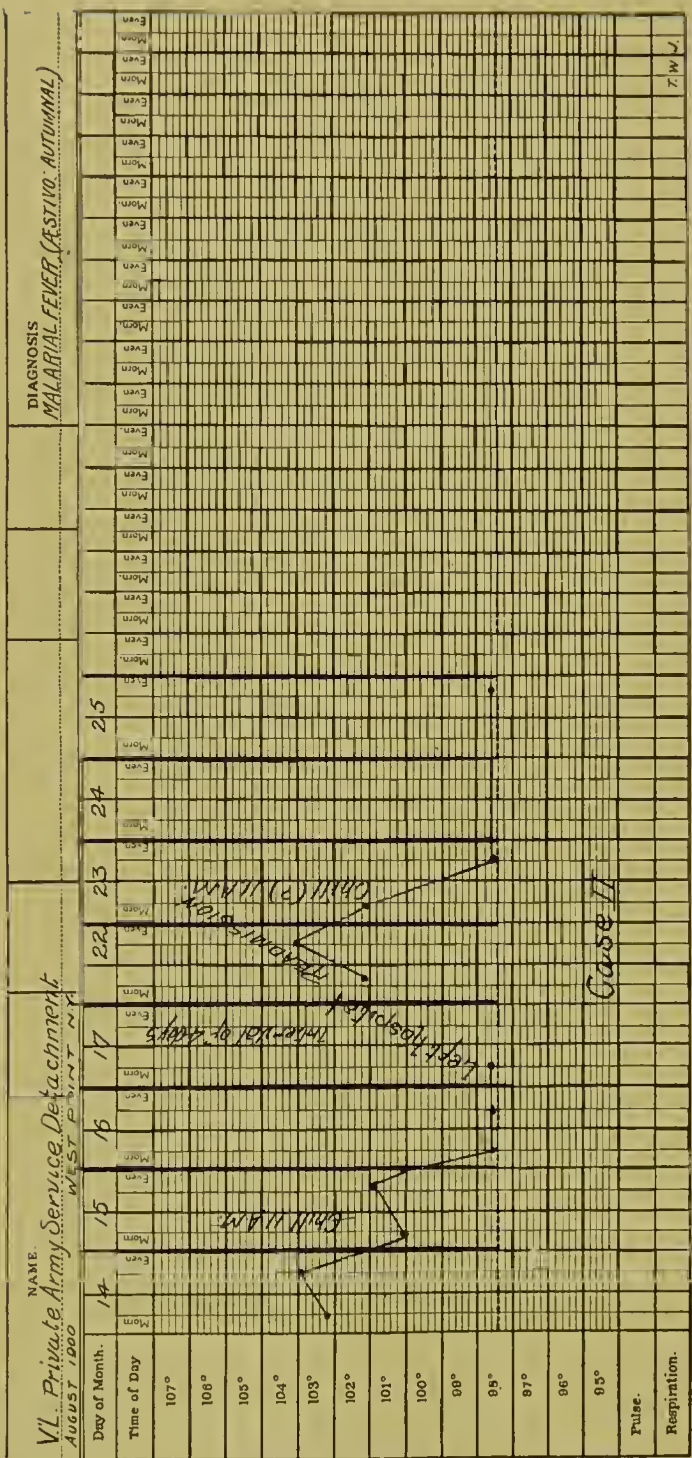


Fig. 46 —Case II.

none of the other patients ever having visited that island or the Philippines.

Case II conforms somewhat to the tertian type of fever described by Italian observers and others, although this conformity is less apparent from the temperature curve than from the patient's statement of chills occurring upon alternate days. In view of the popular belief that chills should occur at such intervals, and in view of the somewhat indefinite ideas prevalent as to what constitutes a chill, it is quite possible that this patient was honestly mistaken. It seems fair to take this view, inasmuch as these chills were not observed at the hospital.

Case IV simulated a quartant intermittent, but neither in Case II nor Case IV did the parasites resemble the benign tertian or quartan organisms. It will be observed that the decline of fever in both cases, following the paroxysms, was less prompt than that which usually occurs in benign infections, and that a crescent was observed in Case IV.

Case V is very similar to many of the cases of continued malarial fever observed in Cuba and the Philippine Islands.

The variety in the type of fever in these cases emphasizes the irregularity of the manifestations of the malignant parasite, and the necessity of correct diagnosis, based less upon the temperature curve than upon the microscopic finding, inasmuch as the treatment accorded the ordinary benign malarial fevers is inadequate in infections of the malignant parasite.

Symptoms and Treatment. During the decades immediately preceding the Spanish war, malarial disease had so nearly disappeared from many parts of the United States that the average practitioner knew comparatively little, from actual observation, of its multiform manifestations. Much of the current belief concerning it was traditional, and it is unfortunately true that ignorance of the disease often led to the use of its name in a diagnostic way, to conceal ignorance of other diseases. It is believed that the importation of tropic malarial disease into the United States during the last seven years alone will supply clinical teachers with material for some time to come.

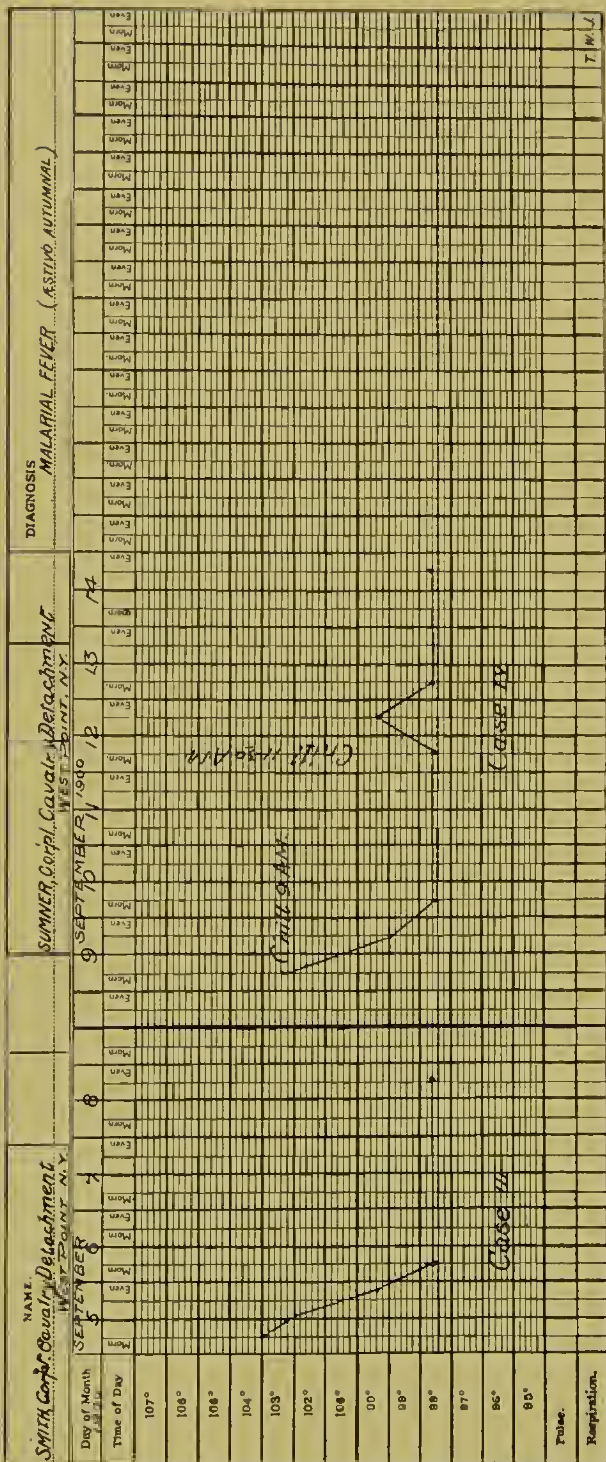


Fig. 47.—Cases III and IV.

During a tour of duty of fourteen months in Cuba, in 1899 and 1900, I had a somewhat exceptional opportunity to observe and study malarial fevers. The results of these observations in more than 1,900 cases were published in the annual report of the Surgeon-General for the year 1900. For nine months following my Cuban service I was stationed at West Point, N. Y., where I saw comparatively few cases, but a large proportion of these were of tropic origin, and here I first had an apportunity to see some of the manifestations of chronic malarial disease. During the months of January, February, and March, 1901, while stationed at the United States General Hospital, at San Francisco, practically all of my cases were of Philippine origin and nearly all were chronic in character. During the remainder of 1901 and 1902 my cases were both acute and chronic and were observed in the Philippines.

In discussing the symptoms of malarial disease we will first study its febrile forms, the malarial fevers, which play an enormous part in the total morbidity and mortality of the tropics, and also in a lesser degree, of the temperate-zone countries of the world.

Statistics are notoriously untrustworthy in view of the inaccuracies of diagnosis practised in the tropics, where practically all diseases associated with fever and attended with any obscurity whatever are classified as malarial. We are accustomed to read in medical prints that the tropic malarial fevers are peculiar in their malignancy and in their manifestations, but extended experience in America, in the Philippine Islands, and in Cuba, convinces me that there is nothing in tropic climate, *per se*, which modifies the expressions of infection with the various hemamebas of malaria. The transportation of malarial subjects from Cuba to the Philippine Islands, and vice versa, does not alter in any respect the character of the disease in these persons. The most virulent and rapidly fatal case of pernicious malarial fever which I recall was observed in one of our northern cities, a community practically free from malarial disease, in the person of an American who had never traveled beyond the limits of his state nor outside of the temperate zone. In this case the human source of infection

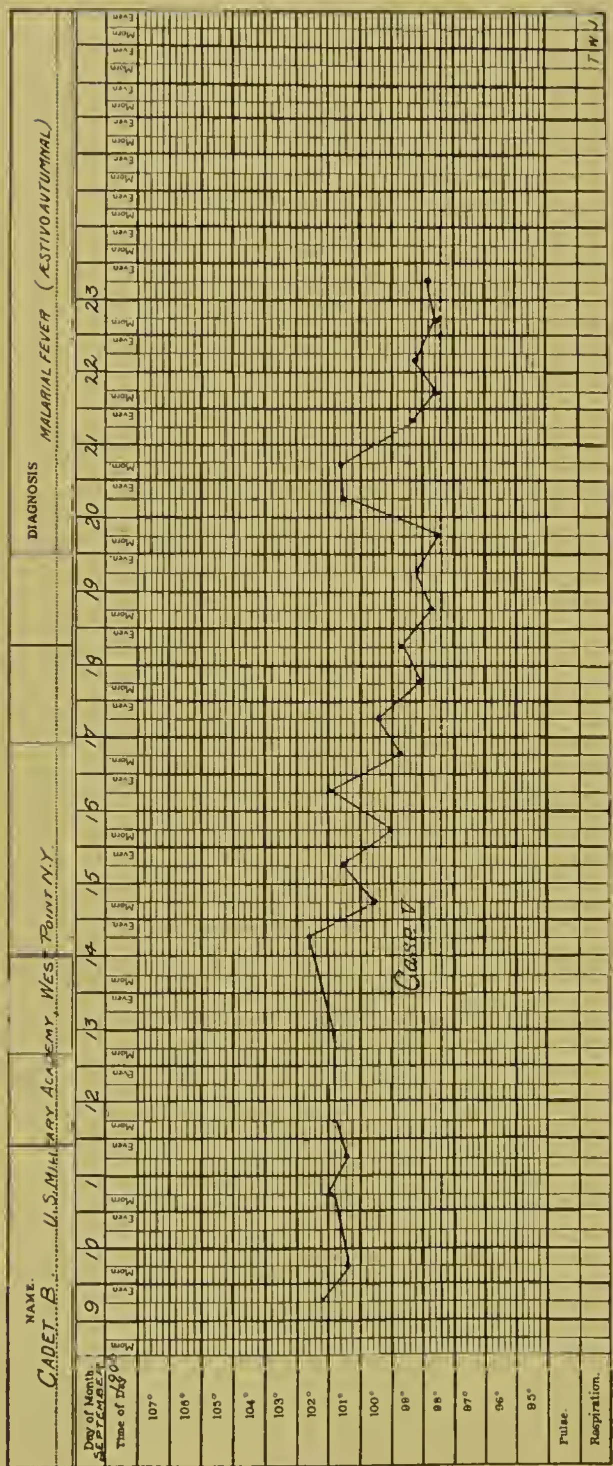

NAME.
CADET B.
U.S. MILITARY ACADEMY, WEST POINT N.Y.
DIAGNOSIS
MALARIAL FEVER (ÆSTIVOAUTUMNAL)
Day of Month.
SEPTEMBER
Time of Day
Morn
Even
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
107°
106°
105°
104°
103°
102°
101°
100°
99°
98°
97°
96°
95°
Pulse.
Respiration.
Case V

Fig. 48.—Case V.

was determined with reasonable certainty to be a recently imported Italian workman who was employed in the same room with the

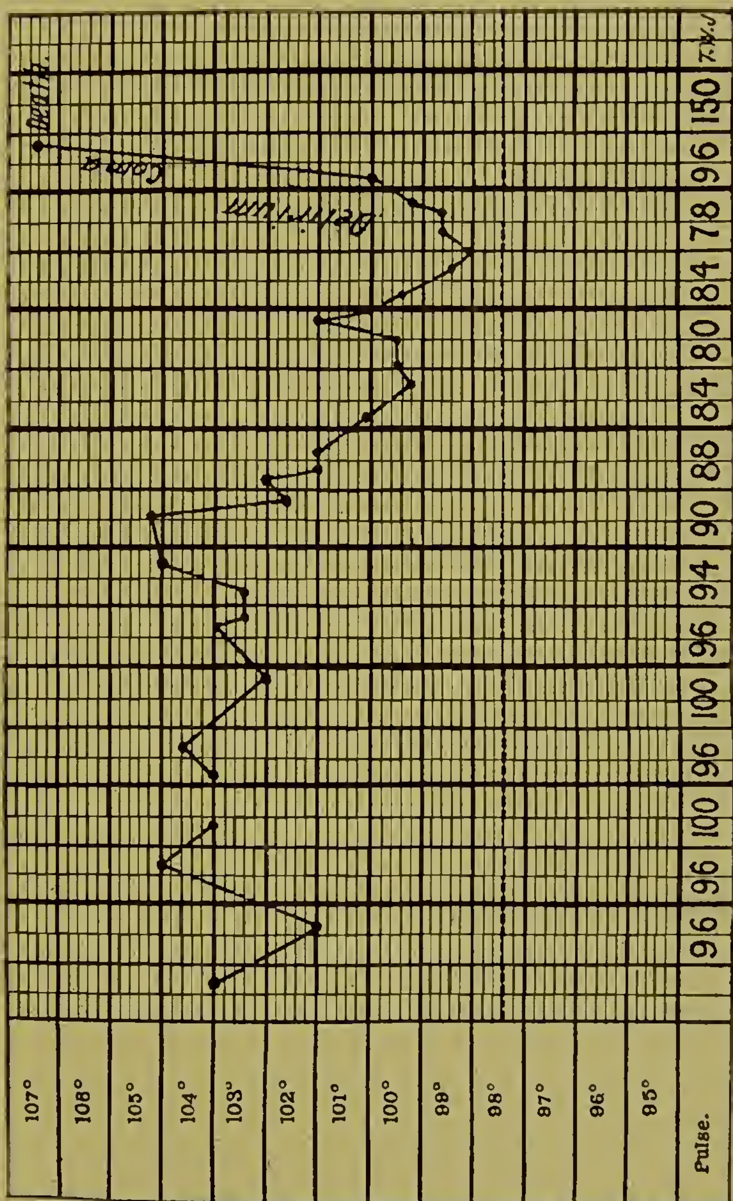


Fig. 49.—Fatal case of pernicious malarial fever, malignant quotidian (estivo-autumnal) parasite. Observed by the author in the United States, in 1904. Compare with chart of J. E., in Cuban series.

American, in a pottery, under conditions favorable for mosquito biting and inoculation. (See chart above.)

Some interesting speculations concerning the effect of mosquito transplantation of latent malaria parasites from the blood of natives of malarious districts, who have doubtless harbored the more or less dormant parasites for a long time, into the blood of a new human host who is in no sense immune to the disease, are suggested by such cases as the one cited above. As indicated in the introductory pages of this work, however, we cannot discuss purely speculative phases.

The greater ratio of pernicious fevers to the total numbers of malarial fever cases observed in the tropics, as compared with the malarial fevers of temperate zones, may be explained by greater exposure to malarial persons and anopheles mosquitos and the consequent greater relative frequency of multiple inoculations.

In explanation of the causes of pernicious cases, F. Löffler, in Modern Clinical Medicine, volume on Infectious. Diseases, p. 239, writes as follows: "The cause of the perniciousness may be ascribed to the intensity of the infection, i.e., to the multitude of the parasites present in the blood. If we consider that Koch found eighty percent. of all the blood corpuscles of a patient attacked by parasites, that, therefore, four-fifths of the blood corpuscles were rendered more or less incapable of performing their physiological function of absorbing oxygen, it becomes conceivable that a severe danger for the entire organism is associated with such conditions." (In a stained specimen of blood from the fatal case mentioned above I find, from examining many fields and averaging them, that fifteen percent. of the red corpuscles were invaded by parasites.—T. W. J.) "As, further, the parasites during their growth absorb the hemoglobin of the blood corpuscles and transform it into melanin, this *corpus de reliquat* must circulate in enormous quantities in the blood during the process of sporulation, and, as a dead mass, give rise to obstructions in a great number of capillaries with all of the ensuing consequences. Besides, however, it is probable that also toxic products of metabolism are present which enter the circulation in the process of sporulation besides melanin. Golgi noted during the process of maturation of the parasites, during the disintegration into

the different particles, that the balance of the blood corpuscles became suddenly pale. From this observation he concluded that a toxin probably becomes liberated simultaneously with sporulation and by the same."

Malarial fever as it occurs in the tropics naturally divides itself into two classes, the *Mild* and the *Severe.*

It is also divided clinically into two great classes, the Intermittent fevers and the Continued or Remittent fevers.

Generally speaking, the Intermittent Fevers are benign and mild and the Continued or Remittent Fevers are severe and grave.

Thayer classifies malarial fevers, safely and conservatively, as: I. The regularly intermittent fevers (a) Tertian fever; (b) Quartan fever (caused by benign parasites).

II. The more irregular fevers: Estivo-autumnal fevers (caused by malignant parasites).

This classification corresponds with the natural division into benign and grave fevers given above and holds good for tropic malarial fevers generally.

Of the regularly intermittent fevers it may be said that they differ not at all, or very little, from the type most familiar to practitioners in the United States.

The benign regularly intermittent malarial fevers are more prevalent in the spring and winter but may be observed at all seasons in the tropics and probably constitute one-half of the total number of malarial fever cases.

As the wet season advances there occurs a progressive increase in the number of cases of continued malarial fever, and during the later months of the rainy season at least fifty percent. of the cases will be found to be of this variety. Such was my observation in Cuba and the Philippine Islands, at least.

The paroxysms of the regularly intermittent fevers usually consist of three stages, Chill, Fever, and Sweat. Of 332 cases observed at Johns Hopkins Hospital 97.5 percent had chills or chilly sensations. In some hundreds of cases observed at Pinar del Rio, Cuba, the percentage giving histories of chills was cer-

tainly smaller, but patients, who upon first questioning did not recall a cold stage, very frequently corrected their statements. The chill may vary from the merest shivering sensation to a pronounced rigor. In those cases without prodromal malaise the chill is more frequently severe.

Promptly following the chill, and indeed setting in before the chilly sensations have terminated, comes the rise in temperature, and at the close of the febrile period occurs the sweat and a critical temperature drop.

Benign Quartan and Tertian fevers bear a close clinical resemblance, the principal difference being in the periods of recurrence.

Quartan fever is marked by a three-stage paroxysm, the chill, variable as to length and severity, the fever, lasting ten or twelve hours or less, and the sweating, which is usually profuse and comes on just before the temperature drops. Just after the chill there appear aching pains in the head, back, arms, and limbs, nausea, vomiting and possibly diarrhea. Any of these symptoms may be absent but they usually occur and persist for some hours. This paroxysm recurs every fourth day about the same hour, although there may be retardation or anticipation of the onset, the paroxysm appearing one or two hours earlier or later than the expected time, owing to delayed or hastened ripening and sporulation of the generation of parasites at work. Between paroxysms the temperature is apt to be subnormal and the patient may feel very well.

Benign *Tertian* fever is also marked by a three-stage paroxsym differing scarcely at all from the one just described. The febrile period is apt to be a little shorter, lasting from a few hours to eight or ten hours. The sensations of cold, of great heat, the headache, limbache and backache, the vomiting, and the looseness of the bowels are identical with those of quartan fever and any or all of them may be present. The interval between paroxysms is two days and the recurrence is at about the same hour. Anticipation or retardation of onset by a few hours may occur as in Quartan fever, and the temperature between paroxysms is apt to be subnormal, the patient feeling very comfortable.

In both varieties of infection, sensations of drowsiness, an inclination to yawning, and slight malaise are frequently present for an hour or so preceding the chill, and in cases in which partial cure has been effected by treatment these symptoms may mark the time of averted or abortive paroxysms.

I believe that all observers will agree that a simplification of terms descriptive of the various forms of malarial fever is highly desirable. To this end, the elimination of terms which are really descriptive of symptoms of intercurrent diseases will greatly contribute. The possibility of the co-existence of malarial fever and some other distinct disease in the same individual must be remembered. My observation has included many such cases. It seems important not to confuse physical signs and symptoms of distinct diseases occurring in the individual at the same time. Often the presence of a leucocytosis, discovered in a search for parasites, leads to the detection of some other disease. Ordinarily the blood of a malarial fever patient does not show an increase of leucocytes.

Estivo-autumnal Malarial Fever may be properly classified into types, in accordance with the predominance of certain symptoms, and in nearly every case it may be shown that these symptoms are evidences of involvement of special organs. Thus, headache and delirium, intestinal pain and diarrhea, may indicate that the brain and its coverings, or the intestines, are being especially invaded by the parasites. In this manner we may use the terms, descriptive of types, Gastralgic, Cardialgic, Comatose, Hemorrhagic, Bilious, etc.

The patient suffering from an attack of estivo-autumnal malarial fever of moderate severity may present the following objective and subjective symptoms: Malaise and anorexia for twenty-four hours followed by an initial chill (which may not be repeated), a coated tongue, which is almost invariably increased in all its dimensions and shows the indentations of the teeth upon its borders, headache, nausea, vomiting, diarrhea, suffusion of the eyes, an icteric condition of skin and sclerotics, pain in the back and limbs, and epistaxis. In short, the picture may simulate

closely the clinical picture of many of the acute infectious diseases, including yellow fever and typhoid. Albumin may be present in the urine, rarely, however, during the first days. The rise of temperature is usually gradual (compared with the rise in the regularly intermittent fevers), and may begin before the chilly stage (if there be one). At the end of twenty-four hours a decline in temperature is usually noted, and if the infection be a mild one, or promptly recognized and treated, a second rise may not occur. Both onset and decline of fever in the estivo-autumnal paroxysms are less sudden than in the regularly intermittent variety. From this point the disease may take on one of several types. If the infection be one of a single crowd of parasites of approximately the same age, and if sufficient quinine, properly timed, either by design or accident, be administered, the initial paroxysm may be the only one. Or, if the quinine be so administered as to destroy all the parasites but a few, and successive doses complete the destruction, the temperature may hover slightly above the normal point for a day or so. Cases of these types are not uncommon, and examples are to be found in the accompanying charts. The temperature curve may show remissions or even intermissions at intervals of from twenty-four to forty-eight hours, either with or without the classical accompaniments of chill and sweat, but in my tropic experiences such regular recurrences of paroxysms, in fevers due to estivo-autumnal parasites, were rare, although some charts were made to show the thermometer readings every two, three or four hours.

It has been contended that the administration of quinine at the outset of a case of fever obscures the type, prevents the occurrence of rhythmic paroxysms and markedly modifies the temperature curve. I do not question the truth of this observation. Indeed, I am convinced that it is correct, but I never feel justified in withholding quinine after a microscopic diagnosis has been established. I am satisfied that a prompt and bold attack upon the disease is essential to complete and permanent cure, especially in infections with the malignant varieties of hemamebas, and I recall with regret cases in which I withheld quinine or temporized

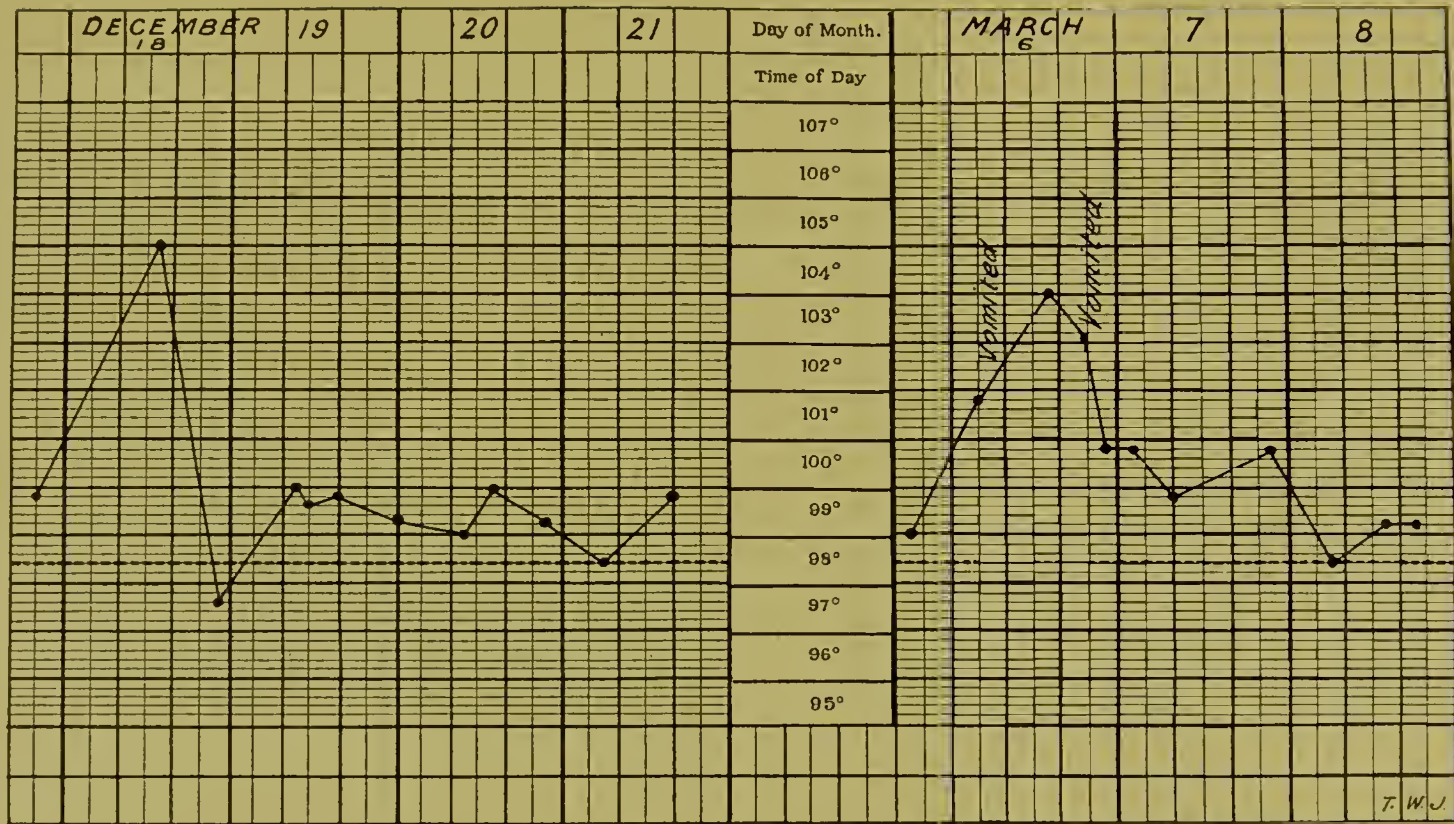


Fig. 50.—Two attacks of fever in a child of 6 years. Malignant tertian (sub-tertian) infection. Observed in the Philippine Islands, 1901-1902.

with small doses of the drug until such multiplication of parasites occurred as to render the cure of the disease difficult and tedious, and in a few cases I attribute the subsequent development of persistent and distressing cachexias to my lack of courage in the therapeutic attack.

Infection with multiple generations, sporulating at all times of the twenty-four hours, is so overwhelmingly the rule that one can readily understand why these fevers are irregular or continued rather than intermittents or remittents.

Fevers of the first described type, viz., those terminating at the end of twenty-four hours, are not infrequently mistaken for benign tertian infections. The true character of the infection, however, may be revealed by the microscope.

If, at the end of the first period, the fever becomes continuous, the group of symptoms commonly described as typhoid gradually appear and the most acute observer is frequently long in doubt as to the true nature of the fever unless he has recourse to the diagnostic microscope.

The clinical picture of a severe case of continued malarial fever is startlingly like that of enteric fever. I cannot better emphasize this truth than by referring to the accompanying charts. Here the therapeutic diagnosis by quinine often fails, but the microscope and the typhoid serum test remain faithful and reliable. It is not my wish to throw the slightest discredit upon the other methods of differential diagnosis. My desire is to emphasize the great similarity of the clinical pictures of enteric fever and continued malarial fever of the estivo-autumnal variety, and the possibility of absolute diagnosis.

Fortunately cases of the last described type do not constitute more than about five percent of the whole, or one in twenty.

It should be borne in mind that the estivo-autumnal infections run the gamut of severity and that very mild cases as well as very severe ones may occur. There is danger that the mild infections may receive inadequate treatment and may assume in later manifestations pernicious types. (See synopsis of fatal Case III, W. B., in group of four fatal cases referred to later. Page 304.)

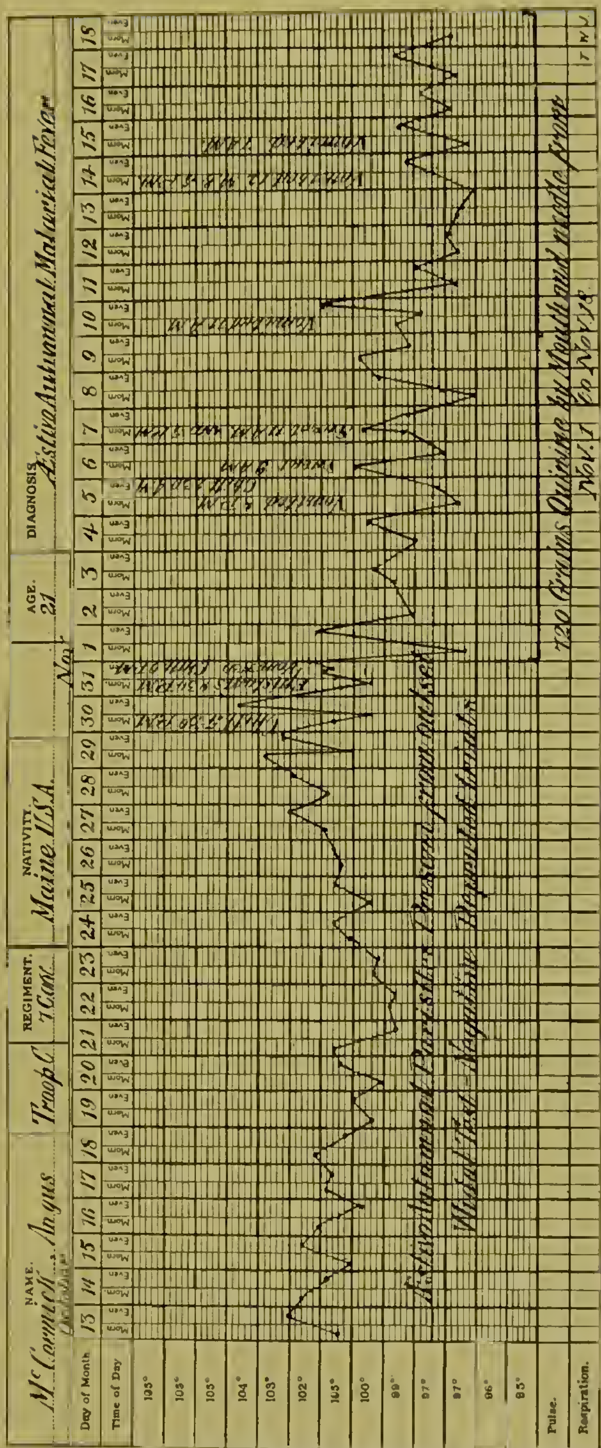

NAME.
Angus
Troop C
REGIMENT.
7 Cav
NATIVITY.
Maine U.S.A.
AGE.
21
DIAGNOSIS
Æstivo Autumnal Malarial Fever
Day of Month
Time of Day
Pulse.
Respiration.

Fig. 51.

The occurrence of combined infections has already been referred to. Among the combinations which I observed in the tropics were those of malarial fever with dysentery, typhoid, tuberculosis (pulmonary), syphilis and venereal diseases of all kinds, and various skin diseases.

The possibility of confusing cases of insolation with malarial fever is to be borne in mind.

The following charts are specimens of estivo-autumnal malarial

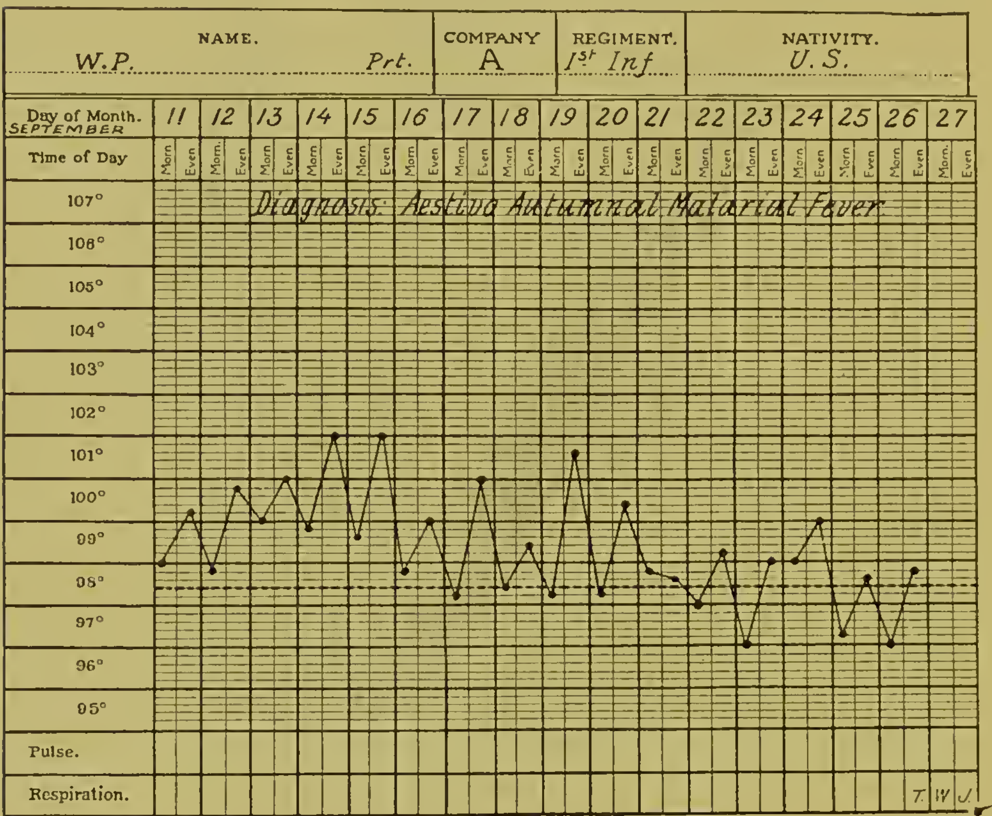


Fig. 52.

fevers observed at Pinar del Rio, Cuba, during the summer and fall of 1899. They might be indefinitely multiplied. All of these cases were microscopically proven and typhoid fever was excluded by the Widal test. They illustrate strikingly, (a) the irregularity of estivo-autumnal fevers; (b) the obstinacy with which these fevers resist quinine; (c) the similitude of estivo-autumnal malarial fevers and typhoid fever. (Cases present

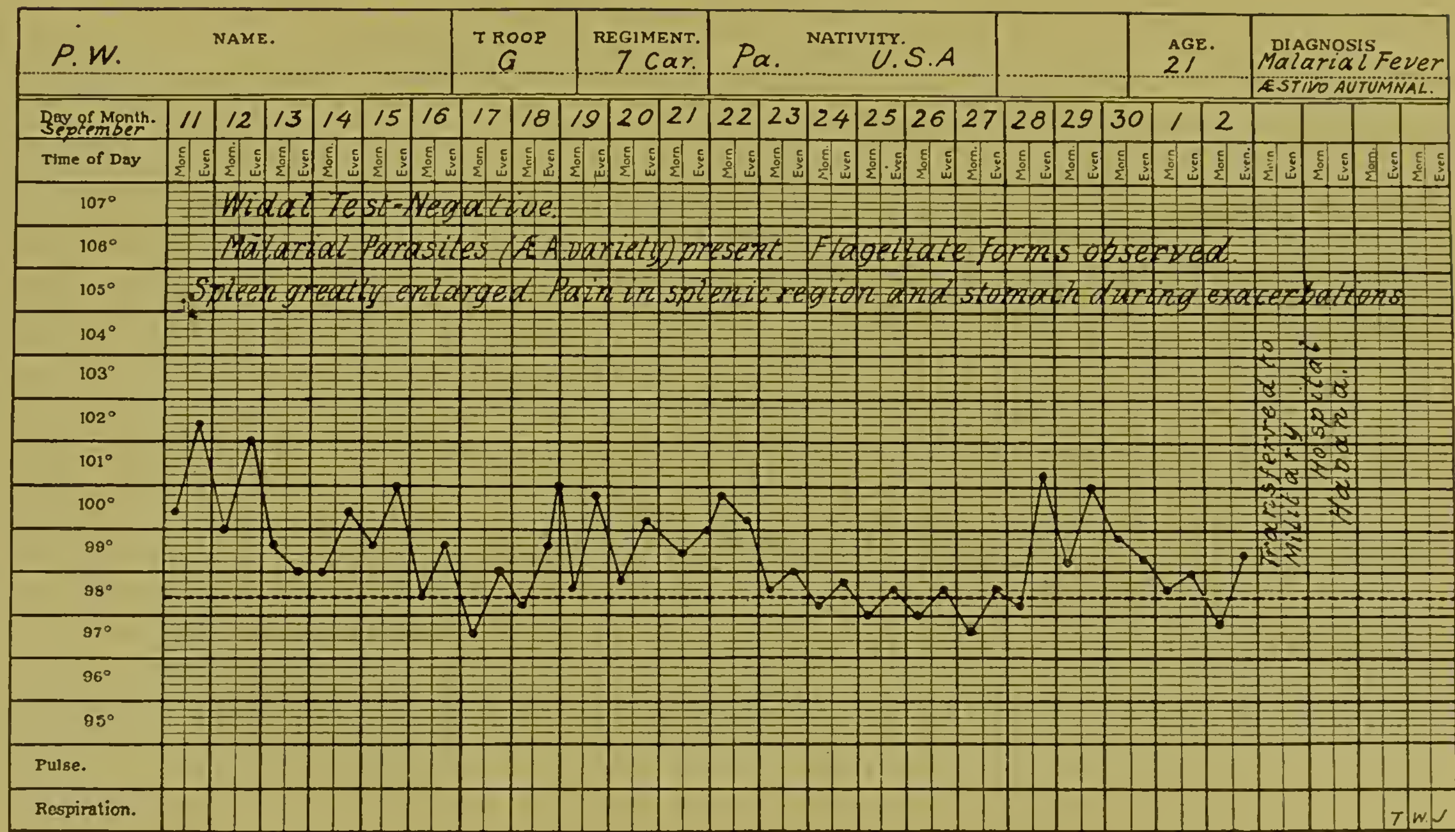

P. W.
NAME.
TROOP G
REGIMENT. 7 Car.
Pa.
NATIVITY. U.S.A
AGE. 21
DIAGNOSIS Malarial Fever
ÆSTIVO AUTUMNAL.
Day of Month. September
11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 1 2
Time of Day
Morn Even
107°
106°
105°
104°
103°
102°
101°
100°
99°
98°
97°
96°
95°
Pulse.
Respiration.
Widal Test-Negative.
Malarial Parasites (Æ A variety) present. Flagellate forms observed.
Spleen greatly enlarged. Pain in splenic region and stomach during exacerbations
Transferred to Military Hospital Habana.
T W J

Fig. 53.

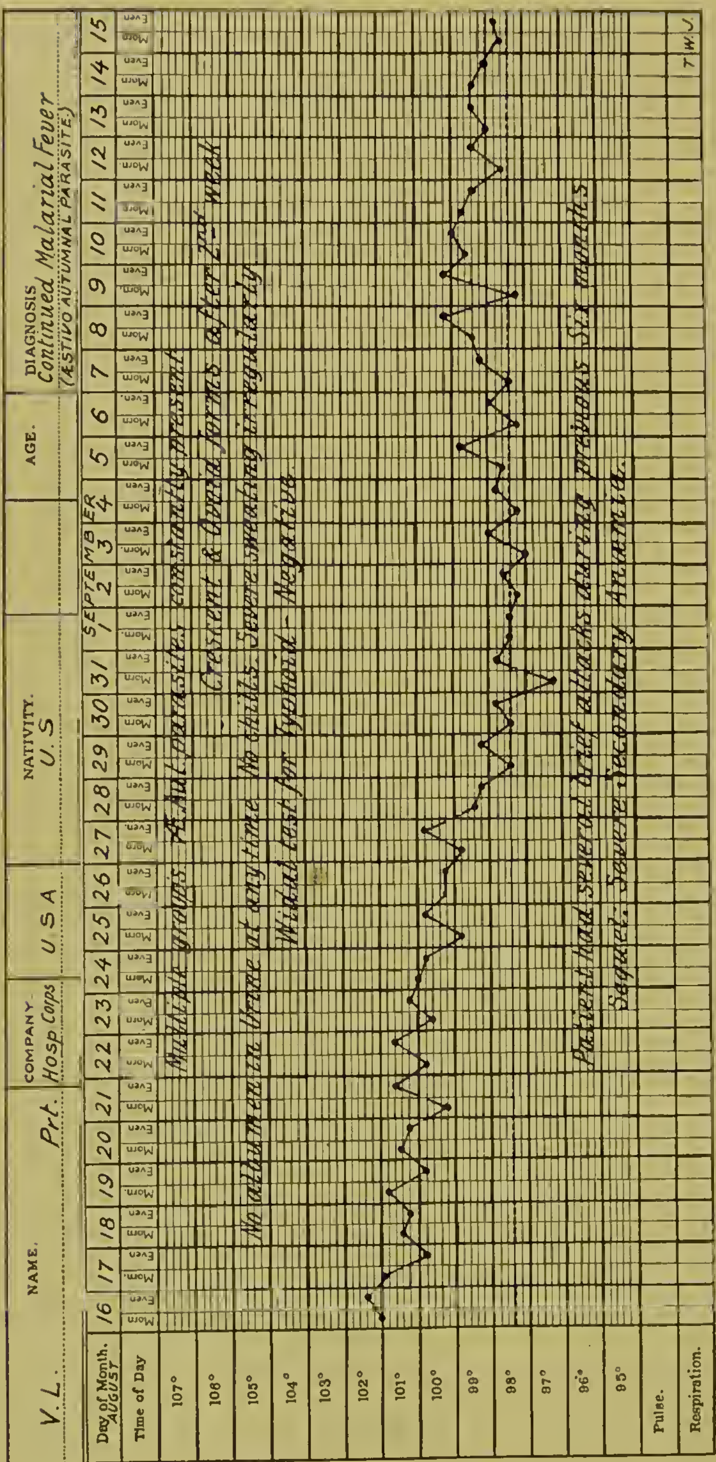

NAME. V. L. Prt.
COMPANY Hosp. Corps U S A
NATIVITY. U. S
AGE.
DIAGNOSIS Continued Malarial Fever (ÆSTIVO AUTUMNAL PARASITE)
Day of Month. AUGUST
SEPTEMBER
Time of Day
Multiple groups Æ. Aut. parasites constantly present
Crescent & Ovoid forms after 2nd week
No albumen in Urine at anytime No chills. Severe sweating irregularly
Widal test for Typhoid - Negative
Patient had several brief attacks during previous Six months
Sequel. Severe Secondary Anaemia.
Pulse.
Respiration.

Fig. 54.

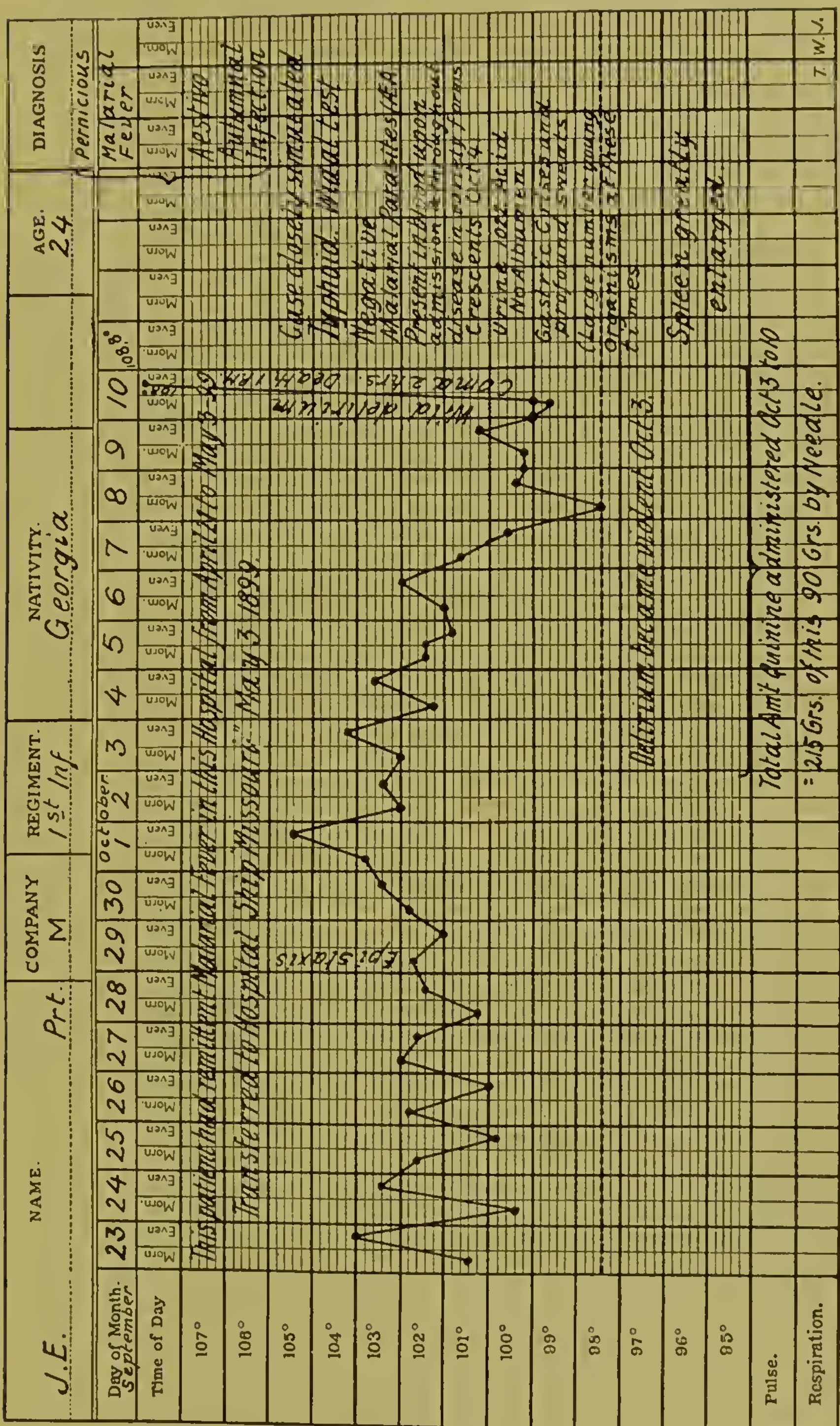

NAME.
J.E.
Prt.
COMPANY
M
REGIMENT.
1st Inf.
NATIVITY.
Georgia
AGE.
24
DIAGNOSIS
Pernicious Malarial Fever
Day of Month. September
October
Time of Day
107°
106°
105°
104°
103°
102°
101°
100°
99°
98°
97°
96°
95°
Pulse.
Respiration.
Epistaxis
Delirium became violent Oct 3.
Spleen greatly enlarged.
Death
T. W. J.

Fig. 55.

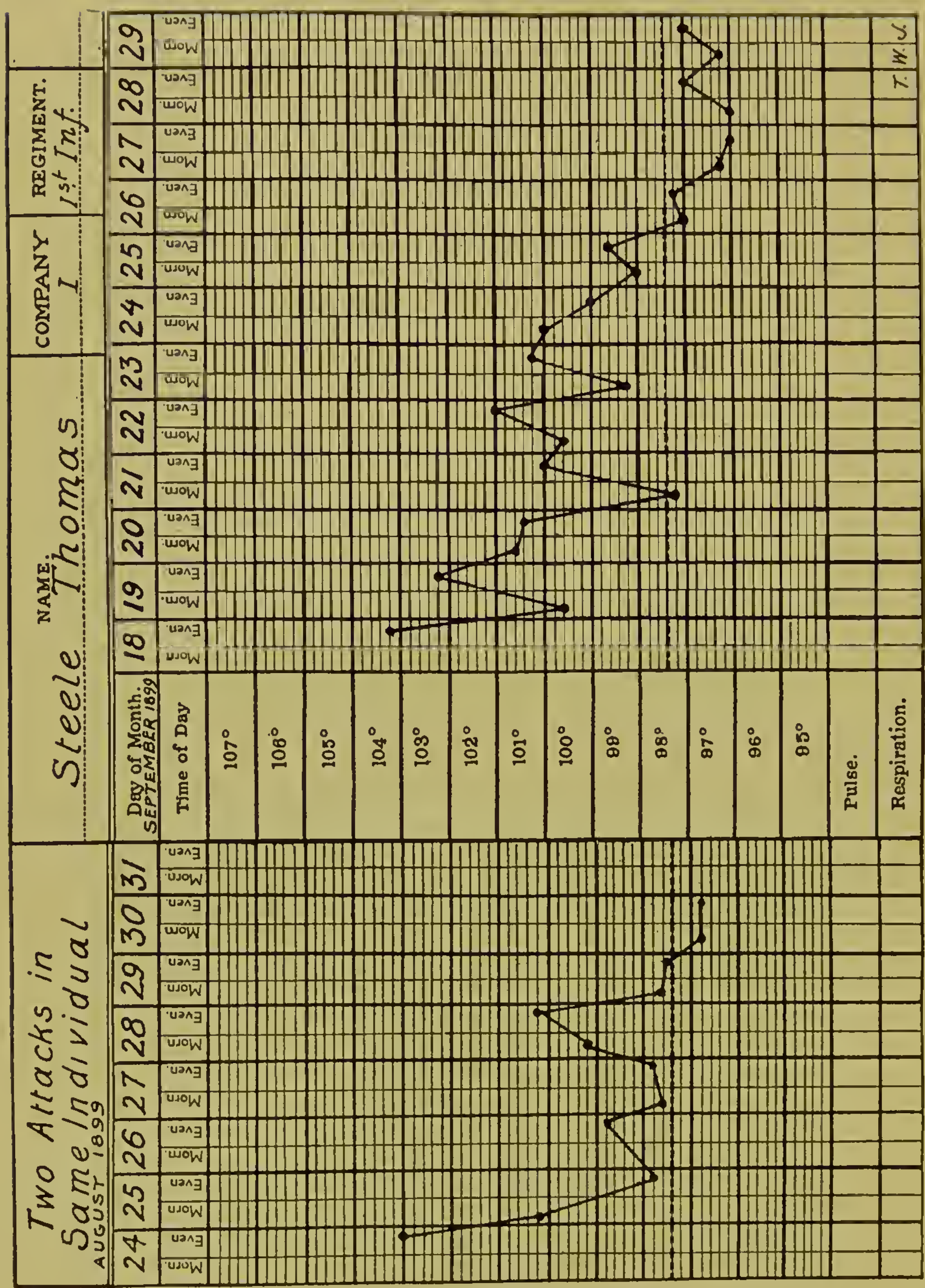

Two Attacks in Same Individual
AUGUST 1899
NAME. Steele Thomas
COMPANY I
REGIMENT. 1st Inf.
Day of Month. SEPTEMBER 1899
Time of Day
107°
106°
105°
104°
103°
102°
101°
100°
99°
98°
97°
96°
95°
Pulse.
Respiration.
T. W. J.

Fig. 56.

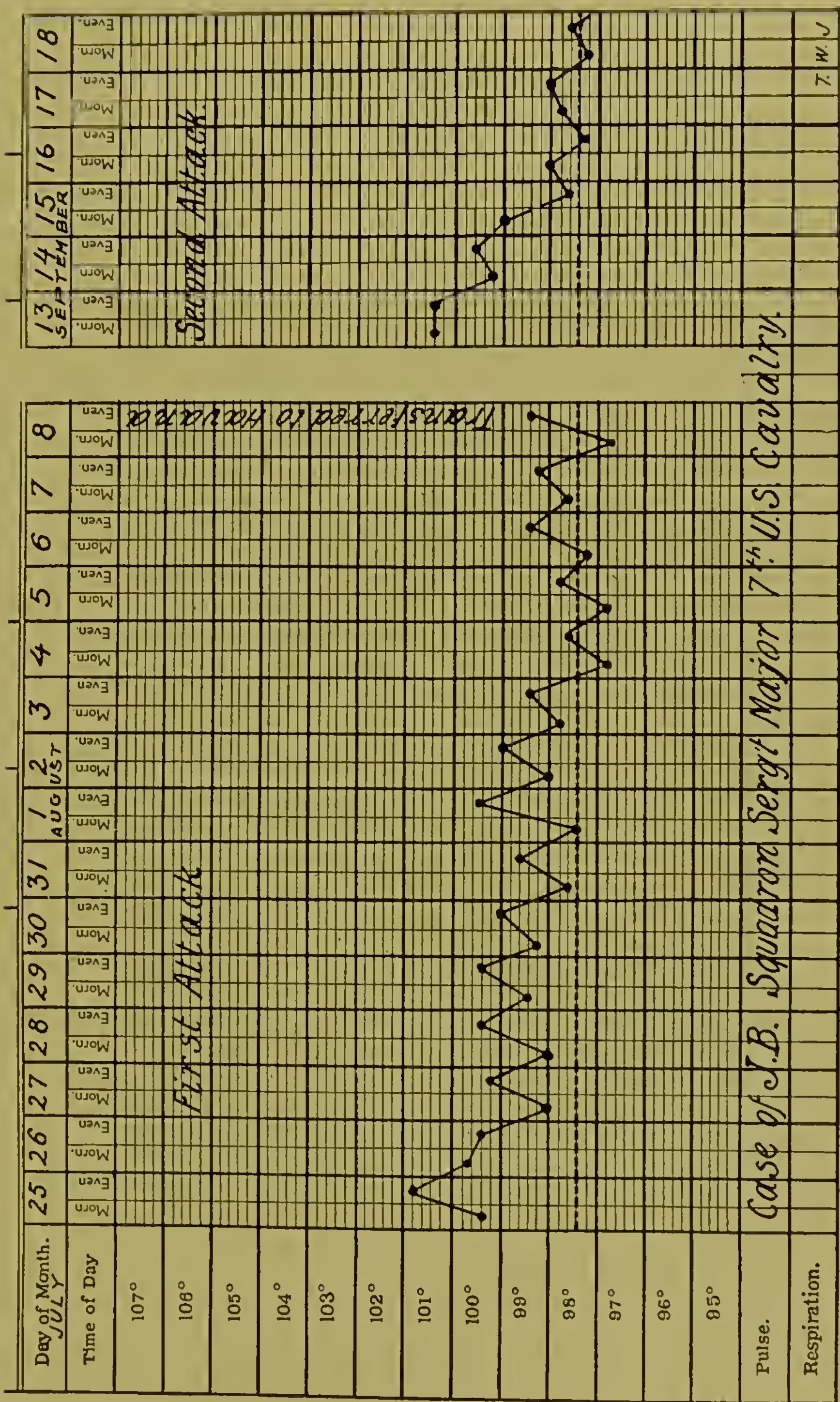

Day of Month.
JULY
Time of Day
107°
106°
105°
104°
103°
102°
101°
100°
99°
98°
97°
96°
95°
Pulse.
Respiration.
AUGUST
SEPTEMBER
First Attack
Second Attack
Transferred to Hospital
Case of J.B. Squadron Serg't Major 7th U.S. Cavalry.
T. W. J.

Fig. 57.

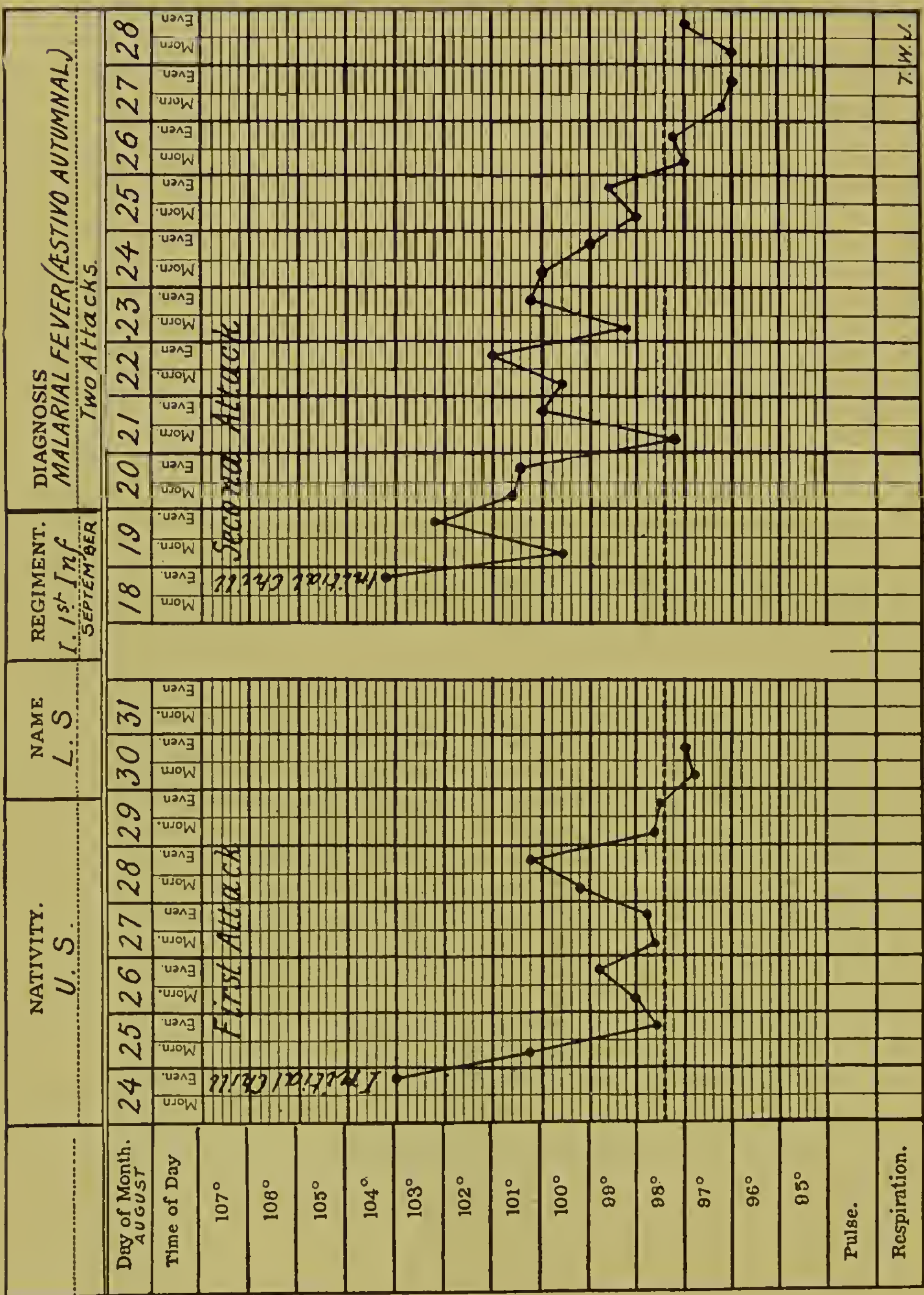

NATIVITY.
U. S.
NAME
L. S
REGIMENT.
I. 1st Inf.
DIAGNOSIS
MALARIAL FEVER (ÆSTIVO AUTUMNAL.)
Two Attacks.
Day of Month. AUGUST
SEPTEMBER
Time of Day
Morn.
Even.
107°
106°
105°
104°
103°
102°
101°
100°
99°
98°
97°
96°
95°
Pulse.
Respiration.
Initial Chill
First Attack
Second Attack
T. W. J.

Fig. 58.

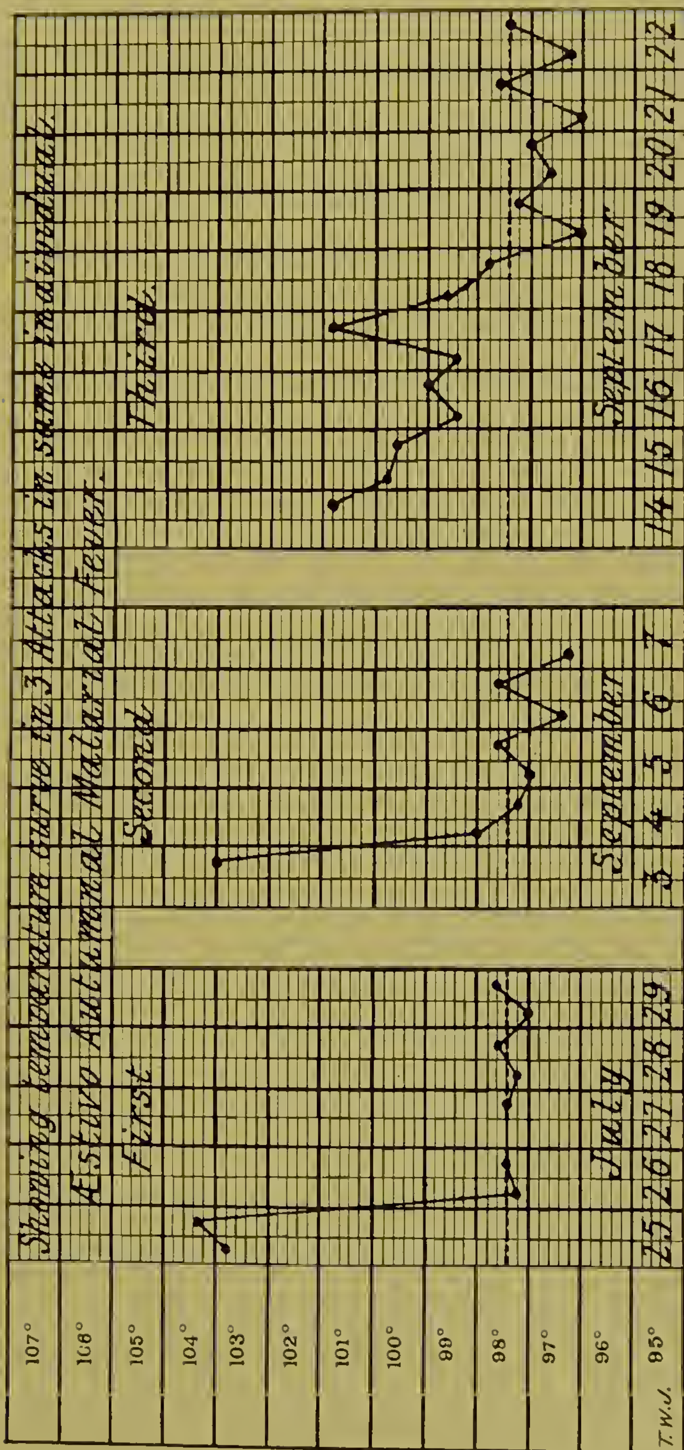

Showing temperature curve in 3 Attacks in same individual.
Æstivo Autumnal Malarial Fever.
First
Second
Third
July
September
September
25 26 27 28 29
3 4 5 6 7
14 15 16 17 18 19 20 21 22
107°
106°
105°
104°
103°
102°
101°
100°
99°
98°
97°
96°
95°
T.W.J.

Fig. 59.

the symptoms of diarrhea, delirium, abdominal pain, epistaxis, etc.)

Were it desirable to classify further, not a few of the cases would of necessity be included under two or more types; for example, the fatal case of J. E. might properly be described as Pernicious, Comatose, Gastralgic, etc. (Page 287.)

Afebrile Malaria exists, probably, more frequently than is generally supposed, particularly in subjects who have experienced several attacks of malarial fever. It rarely occurs except as a sequel of the latter. Its diagnosis can only be made microscopically. I have observed a number of cases, in nearly all of which the parasite was of the estivo-autumnal variety. The symptoms are malaise, headache, nausea and sometimes vomiting, occurring with an abortive chill or sweat.

As I have elsewhere remarked (American Medicine, July 1, 1905), "there is a prevalent tendency to consider only the febrile manifestations of malarial disease and to overestimate the diagnostic significance of periodic paroxysms. It must be admitted that both fever and periodic paroxysms are usually present in any case of acute malarial disease, but it must also be borne in mind that both are frequently absent in chronic malarial disease. The microscope has superseded the thermometer as a diagnostic instrument in this disease and the terms intermittent and remittent have lost something of their former significance. It can no longer be doubted that malarial disease may persist for a long time without rise of temperature or the occurrence of recognizable paroxysms. A number of times in my experience, blood examinations with positive results have been made in cases in which the sum of the symptoms was best expressed by the term "debility," and in which no febrile manifestations were present, the patient being entirely without suspicion of malarial disease, having recognized no paroxysms. Much oftener have the parasites been found, in greater or less profusion, in the blood of those who suffered from the usual forms of malarial infection months before, and who were without suspicion that they were suffering from afebrile malarial disease. I would invite consideration to a

common form of expression of malarial infection in the Philippine Islands, often due to the afebrile type of the disease, which usually receives scant attention. This is *diarrhea*. There are many, doubtless, who do not admit the occurrence of diarrhea as an expression of malarial infection, and I shall endeavor to establish the fact that it does occur. Authorities are somewhat silent upon this point. Manson, in his "Tropical Diseases" (page 114), writes as follows: "We find that the subjects of malarial cachexia are apt to be dyspeptic; to suffer from morning diarrhea, at first of dark, bilious, later, perhaps, of pale, copious, and frothy stools." Again (on page 118), under the head of sequels: "Dysenteric conditions and forms of diarrhea may supervene at any time and rapidly carry off the subject of advanced malarial cachexia."

Osler remarks, under the head of estivo-autumnal fever, that "intestinal symptoms are usually absent" (page 168), but under the pernicious malarial fevers, states that "there may be most severe diarrhea, the attack assuming a choleriform nature" (page 168). Under malarial cachexia he makes no reference to the condition of diarrhea. He admits, however, that many of the malarial fevers require studying anew. Under the causes of diarrhea, Munson, in his "Military Hygiene" (page 664), does not mention malarial infection. I have been unable to find any reference to diarrhea as an expression of malarial infection in the circulars on tropic diseases, published by the Medical Department of the Army in the Philippine Islands.

It is fair, then, to assume that diarrhea is not generally considered as an expression of malarial disease. In Cuba the occurrence of diarrhea in cases of malarial infection (chiefly acute cases) was noted, but the proportion of cases showing this symptom was not recorded. I quote the following from my paper "Twelve Months' Observations of the Cuban Malarial Fevers in Pinar del Rio Province" (1904 studied cases), published in the annual report of the Surgeon-General for 1900: "It is frequently difficult to decide whether or not dysenteries, apparently of the simple catarrhal variety, which occur coincidently with malarial fever, are in any way referable to the latter disease. Their apparent

cure, in certain cases, by quinine strongly points to a relationship between the conditions. The ambulatory fever cases are more apt to present this symptom. No cases of amebic dysentery or liver abscess have been observed at Pinar del Rio." Again, "It is well known that digestive derangement is fairly constant in all malarial fevers."

While in charge of two medical wards of forty beds each at the United States General Hospital at San Francisco, I began first to observe that in a very large proportion of the chronic malarial cases returned from the Philippines, the patients had diarrhea.

Upon admission to the hospital the blood and stools, in each medical case, received careful microscopic scrutiny at the hands of an excellent pathologist (Dr. C. F. Craig). These procedures were repeated as often as requested by the surgeon, and the examination for both blood and intestinal parasites was exhaustive. Blood counts and hemoglobin percentages were also freely furnished. The stools in many malarial cases contained *Ameba dysenteriæ*, the parasites, eggs or segments of *Ascaris lumbricoides*, *Ankylostomum duodenale*, or *Teniæ*. On the other hand, the blood in many of the patients suffering from these intestinal parasites contained malaria parasites, even when none of the ordinary manifestations of the latter organism were present. After eliminating all of these cases of combined infection there remained not a small percentage of cases of chronic malarial infection with diarrhea, in which the causative organisms of diarrhea just mentioned were not found in the stools upon repeated examinations. It was likewise observed that these diarrheas were extremely irresponsive to the most careful dieting, intestinal antiseptics and opium preparations, but frequently responded to quinine enemas. We did not interpret this fact to mean that the cases were, after all, cases of amebic dysentery, and that the benefits were due to destruction of amebas in the colon by the quinine enemas. It was believed, rather, that the absorption of the quinine solution was destructive to the malaria parasites within the smaller intestinal blood vessels. The fact that cinchonism followed these enemas proved that absorption occurred and it was often

difficult to secure cinchonism by the oral administration of quinine in these same cases, absorption undoubtedly being interfered with by the chronic catarrhal condition of stomach and small intestine. In this connection the observations of Marchiafava and Barker, as pointed out by Osler, that the gastro-intestinal mucosa is specially invaded by the malaria parasites in a certain type of pernicious malarial fever and that actual thrombosis of the small vessels, with superficial ulceration and necrosis, occurs, are interesting. If this extreme condition occurs in pernicious cases it is fair to presume a milder degree of the same invasion of the mucosa in chronic infections. It is, however, possible to explain the occurrence of diarrhea in malarial infections in other ways.

The constant supply of impoverished blood, innutritious and with lessened oxygen-carrying capacity, to such organs as the stomach and intestine, cannot fail to pervert the function of digestion, and one of the commonest forms of such perversion of the digestive function is diarrhea.

The destruction of red blood cells by malaria parasites, and the presence in the blood plasma of hemoglobin, pigment, and corpuscular materials, which under ordinary circumstances are largely converted into bile pigment, produce an actual polycholia. Bile flow in the intestine is known to promote peristalsis, to stimulate a watery flow from the intestinal follicles, and to act as an intestinal lubricant. These functions carried on to an abnormal extent constitute a pathologic condition, viz., diarrhea.

These facts seem sufficient in explanation of the occurrence of diarrhea in malarial infections, acute and chronic.

The following tables are compiled from 119 cases of malarial disease personally observed in the Philippine Islands during the year 1901 to 1902. Of this number ninety-eight were studied at the Base Hospital, at Santa Cruz, Laguna Province, and twenty-one at the Military Hospital, Naic, Cavite Province.

Attention is invited to the fact that no cases of diarrhea or dysentery due to amebas, ankylostoma, teniæ, or other intestinal parasites are included in these tables. Such combined infections,

particularly amebic dysentery and malarial disease, were frequently encountered, but were carefully excluded from this consideration and these tables. All diagnoses are, of course, microscopic.

Attention is especially invited to the fact that the subjects of the cases here reported were all exempt from the exposures of recent field service, with such predisposing and exciting causes as hard campaigning, restricted rations and impure water. The garrison ration, upon which all of these patients were subsisting when admitted to hospital, included fresh beef and vegetables, and water of unquestionable purity, sterilized, such pure water, indeed, as the dwellers in our American cities rarely, if ever, enjoy.

TABLE I.—SANTA CRUZ, LAGUNA, CASES.

	Tertian benign.	Tertian benign and estivo-autumnal.	Estivo-autumnal.	Variety undetermined.	Total.
Malarial infections	70	1	20	7	98
Malarial infections with diarrhea	13	1	9	4	27

Percentage of all malarial cases with diarrhea 27½
Percentage of estivo-autumnal cases with diarrhea 45
Percentage of double infections with diarrhea 100
Percentage of benign tertians with diarrhea . . . . 18$\frac{4}{7}$
Percentage of cases of undetermined variety with diarrhea . . 57$\frac{1}{7}$

NAIC, CAVITE, CASES.

	Tertian benign.	Tertian benign and estivo-autumnal.	Estivo-autumnal.	Variety undetermined.	Total.
Malarial infections	13	0	4	4	21
Malarial infections with diarrhea	4	0	2	0	6

Percentage of all malarial cases with diarrhea . . . . 28$\frac{1}{10}$
Percentage of estivo-autumnal cases with diarrhea 50
Percentage of double infections with diarrhea 0
Percentage of benign tertians with diarrhea . . . . 30$\frac{5}{8}$
Percentage of cases of undetermined variety with diarrhea . . 0

The similarity of the percentages in these two series of cases, observed during different seasons of the year and at points many miles apart, one inland, the other upon the seacoast, is certainly striking.

I have no hesitancy in expressing the opinion that many cases of diarrhea and gastro-intestinal catarrh are constantly occurring in which the real cause, viz., a malarial infection, is overlooked. Not forgetting the numerous waterborne causes of digestive and diarrheal disease and their prevalence, it is believed that the gastro-intestinal tracts of American soldiers serving in our tropic possessions are damaged as greatly by malarial infections, in the manner explained, as by improper diets and the much-abused and alleged irrational army ration.

I am pleased to find in the excellent work of Dr. Craig upon "Estivo-autumnal Malaria," which reached me after the compilation of these tables, confirmation of some of my statements. Upon page 116, he mentions nausea, vomiting, pain over the stomach, and diarrhea as common symptoms, occurring as a rule during paroxysms. Under "Latent or Masked Infections" (footnote, page 167), appears the following: "Since writing the section upon 'Latent and Masked Estivo-autumnal Fever,' I have kept a record of the cases in which malarial parasites were present in the blood, but diagnosis other than malarial, and in nine months at the United States Army General Hospital, at San Francisco, I found 172 such cases; (131 were estivo-autumnal.—T. W. J.) Of these 131 cases, forty-three were diagnosed as chronic dysentery, fifteen as chronic diarrhea, in thirty-four no diagnosis was recorded, while the remaining thirty-nine were variously diagnosed." Upon page 179, under sequels, he states that: "As a result of the localization of the malaria parasites in the mucous membrane of the stomach, and in the intestine, a true acute or chronic ulcerative enteritis and the formation of gastric ulcers may occur."

I will report briefly a case which came under my observation and which may be described as a type of the atypical. It illustrates a number of the points cited and is not included in the preceding tables:

Recruit L. R. B., Troop A., Sixth Cavalry; just arrived in Philippine Islands from the United States. Previous history negative. The patient was never aware of malarial infection nor treated for it. He was taken ill early on the morning of March 6, 1902, with vomiting, diarrhea, and epigastric pain. While at stool he had marked chilliness and shivering, with copious perspiration. He was immediately admitted to the hospital. Temperature was normal. By the following morning the sclerotics were icteric and the skin of the chest and abdomen was distinctly yellow. Blood examinations, made March 7, 9, 11 and 13, were as follows:

TABLE II.

Date.	Parasites.	Pigment.	Leucocytes.	Lens.
March 7.[1]	Few hyaline motile parasites, variety uncertain.	Present.	Reduced.	$\frac{1}{12}$
" 9.[1]	Numerous hyaline forms.	Recent black pigment.	Leukopenia	$\frac{1}{12}$
" 11.[1]	Many intracorpuscular parasites, motile, hyaline and pigmented; 1 large presporulating form. Benign tertian.	Black pigment, free and included in leucocytes.	Leukopenia	$\frac{1}{12}$
" 13.[2]	Parasites extremely numerous. Sporulating forms. Benign tertian.	Pigment as before.	Leukopenia	$\frac{1}{12}$

The patient felt well from a few hours after admission to the hospital. His temperature was taken at intervals of six hours, and was invariably normal or subnormal—never elevated. There was no tenderness in the regions of the gall bladder and spleen. No chill, vomiting, nor diarrhea occurred during the patient's stay in the hospital, but slight sweating occurred once or twice. The treatment was as follows: Confinement to bed, liquid diet, an initial dose of magnesium sulphate with camphorated tincture of opium for relief of epigastric pain. Upon the appearance of

[1] Temperature normal. Has had no quinine.

[2] Temperature normal. Quinine ordered for first time.

jaundice, sodium phosphate was administered. No quinine was given until March 13, when gram doses every three hours were ordered. Under this treatment all intracorpuscular parasites disappeared from the circulation in three days, fragmented dead parasites and pigment persisting for some days. Until after the blood was examined the case was considered one of acute gastro-enteritis or acute cholecystitis.

This case illustrates the facts that elevation of temperature and periodic paroxysms are *not always present*, even in benign tertian infections. Also that gastric and intestinal disturbances are sometimes the only expressions, even in an original case, and that while objective symptoms sometimes disappear upon confinement to bed, parasites will persist in the blood, and blood destruction will continue until enough quinine is given to destroy them, an accomplishment frequently more difficult than in the case here cited.

Naturally, malarial cachexia is frequently observed in the subjects of repeated estivo-autumnal infections. It is almost invariably associated with a secondary anemia, often rather profound in degree. It is in this condition that the administration of arsenic is valuable. I have found arsenic utterly valueless in the treatment of acute malarial fevers.

The condition of *Malarial Cachexia* presents so many and such varied aspects as to render description difficult. It is intimately associated with malarial anemia and the symptoms are principally those of anemia. A constant condition is the presence of parasites in the circulation. They may not be easily discovered in the peripheral circulation but the other microscopic evidences of hemamebas are present in the blood, and parasites are usually detectable by patient search. The skin is usually sallow and the buccal and conjunctival mucosa pale. The sclerotics are pearly or yellow tinged. Splenic and hepatic swelling, either or both, may be present but are not necessarily marked. Frequent attacks of irregular fever are common but fever is not a necessary accompaniment of the condition. Shortness of breath, aching back and limbs, headache, severe and irresponsive to all drugs but

quinine and morphine, neuralgias, irritability of temper and mental apathy are all symptoms of the condition and all are more or less periodic, quotidian or tertian; or they are readily precipitated by exposure, unusual stress or exertion, and physical or mental fatigue.

These symptoms are extremely variable in degree and resistant to treatment. The digestive and nervous systems are affected both functionally, and, in long standing cases, organically. Neuritis sometimes occurs. I have never observed any skin affections referable to malaria other than herpes and urticaria. A dermatitis medicamentosa is sometimes produced by quinine but cannot be considered an expression of malaria.

Manson explains the occurrence of malarial cachexia without fever by saying that "just as the habitual use of opium produces a species of chronic poisoning without narcosis, so the habitual presence of the malaria toxin may produce its peculiar cachexia without giving rise to fever."

Chronic nephritis as a result of malarial cachexia is common, according to resident medical observers in the tropics. The condition of malarial cachexia promotes the progress in its subjects of almost every intercurrent disease, lowered resisting power being the inevitable result of prolonged anemia.

Dropsical effusions of cardiac origin are occasionally noted, the myocardium degenerating from the altered nutrition incident to anemia. Procreative power in both male and female malarial subjects is generally admitted to be weakened, but whether or not malaria parasites are actually found in the circulation of the unborn fetus or of the newborn child is a disputed question. There would seem to be no adequate obstacle to the passing of the parasites from mother to child in the blood current and the actual finding of grown parasites in the blood of a child within an hour or two after birth should settle the dispute, as the time necessary for the growth of any parasite after introduction into the blood current by the mosquito is never so brief as this period.

I am impressed with the frequency with which mild cases of malarial cachexia are overlooked by medical men. While this

phase of malarial disease is difficult to treat satisfactorily, particularly when caused by estivo-autumnal parasites, it should not be despaired of. If the earlier and milder forms were recognized the cure of these cases would be more common. Residence in the tropics in itself does not constitute an actual cause of malarial cachexia but, rather, a favorable condition for its existence and continuance. In the tropics there are the dangers of re-infection, even from mosquitos which have fed upon the patient himself, (as has been pointed out elsewhere), the enervating influences of nostalgia and continued hot weather, and often the difficulty of securing proper and nourishing food. Removal to temperate home shores separates one from the mosquitos, the heat and the homesickness, but it does not separate him from the parasites within him, to which he is playing host, and unless active and continued warfare be made upon the parasites within the patient the cachexia will continue, modified, perhaps, but still real and menacing to comfort and life. Many such cases may be found among returned soldiers who have served in the tropics.

These individuals also serve to infect communities, the only other necessary factor being the anopheles mosquito. It is important, therefore, to the patient and to the community that these cases be cured. The secret of success is the *adequate*, *judicious* and *persistent* use of quinine to destroy parasites, and the repair of blood by iron, arsenic and similar reconstructives, supplemented by ample nourishment and rest.

The spleen is usually demonstrable in cases lasting four or five days, and in some instances is the seat of considerable pain. (See chart in case of P. W., page 285.)

Malarial hepatitis was observed in one of my cases of recurring estivo-autumnal fever in Cuba, but I believe it to be a less common expression of tropic malarial disease than is usually supposed. Jaundice of a moderate degree is rather frequently observed but in my tropic experience severe catarrhal jaundice was a much less frequent complication of malarial fevers than in a similar number of typhoid fever cases, observed in the military camps in the United States in 1898. The jaundice in

malarial fever cases is in proportion to the amount of red cell destruction, but, as Thayer points out, it is probably due to an excessive production of bile, the result of an effort on the part of the liver to dispose of the excessive amount of pigment deposited in that organ.

Contrary to the experience of recent writers, the urine in our tropic malarial fever cases rarely contained albumin. Even in our gravest cases its occurrence was exceptional.

Hemoglobinuria was observed but infrequently and never as a postmalarial affection. No cases due to quinine administration were observed.

The teachings concerning *Malarial Hemoglobinuria*, paroxysmal hemoglobinuria, or black-water fever, as the condition is variously called, are so contradictory and the subject is one of such ardent dispute at present that I hesitate to do more than describe it.

The condition may be described as a syndrome occurring in the subjects of chronic malarial infection or malarial cachexia and never as an initial event. It is introduced by a severe chill and marked by the presence of hemoglobin in the urine, giving the latter a bright red or dark brown color; by fever and marked jaundice and usually by vomiting. It may be postparoxsymal and is not necessarily fatal, but may be followed by severe acute nephritis. Suppression of urine may supervene and cause death. It is an extremely grave affection. It is most frequently encountered in tropical Africa and is but little known in the American tropics, although certain parts of the Southern Mississippi valley in the United States annually report numbers of cases. It must not be confused with hematuria, which condition may arise from many causes, including the tropical infection Bilharzia, and it may be distinguished by microscopic examination of the urine which will show the presence of red blood cells in hematuria and few or none in true hemoglobinuria.

By many observers, including Koch, and apparently upon strong evidence, it has been alleged that the condition is most frequently caused by quinine administration. For the time being, at least,

we can accept the conclusions of Stephens and Christopher, in "The Practical Study of Malaria" (1904), as representing the latest and most advanced teachings. They maintain that while cases of hemoglobinuria do rarely occur in persons who have not been treated by quinine this drug is the common cause of the attacks. They contend that it is not the quinine itself but the blood condition of the patient which is the determining factor whether quinine will produce an attack. "Black-water fever is then a quinine intoxication, but it is something more. It occurs only in those who have previously suffered from malaria, and in fact there is considerable evidence to show that it occurs frequently in direct association with a malarial infection." In answer to the common denial that black-water fever is malarial at all, they show that in 100 cases microscopically studied, parasites were found in the blood the day before the attack in ninety-five percent., on the day of the attack in seventy percent., and on the day after the attack in twenty percent. of the cases. In a series of cases which they examined in British Central Africa parasites were found in only 12.5 percent. but by using the other two microscopic tests (the presence of pigmented leucocytes and the increased percentage of large mononuclear leucocytes), they proved that 93.7 percent. of the cases were malarial. I thoroughly agree with their conclusion that "it is illogical to abstain from quinine in malaria; on the contrary its adequate administration would prevent the occurrence of these attacks." Manson writes as follows concerning a well-known phenomonon: "It is a striking fact that the malaria parasites, which may be present before and at the outset of a hemoglobinuric attack, generally disappear from the blood during the progress of the hemoglobinuria, and that without quinine, and further, that a hemoglobinuria may terminate for good a chronic malarial infection. Hemoglobinuria, or, rather, the sudden destruction of all the parasite-infected corpuscles, and consequently of the included parasites, would seem, therefore, to be a method of spontaneous cure of a malarial infection." (Tropical Diseases, p. 91.)

In the series of 1904 cases of Cuban Malarial fever to which

I have referred before, but four deaths occurred in the hospital, or so long as the patients remained within the sphere of knowledge of my associates and myself. As to how many of them, after removal from the tropics, eventually succumbed to malarial disease expressed either by acute recurrence of fever, by post-malarial anemia or by organic changes in vital organs resultant upon the destructive or toxic effects of malaria parasites, nothing can be stated or ascertained.

Of the four fatal cases, one is that of J. E. whose chart is shown herewith, giving the principal points of the history and symptoms as well as the temperature curve. (See page 287.)

The prominent symptoms in the three other fatal cases are noted below.

I. M. J.—Pernicious malarial fever (e-a. parasite), duration, four days, high temperature, wild delirium, profuse sweating, coma thirty-six hours, ending in death.

II. W. W.—Pernicious malarial fever (e-a. parasite), duration eighteen days, high temperature, no delirium, general purpura appeared upon ninth day, bleeding from gums, left hemiplegia, coma (brief), preceding death.

III. W. B.—Pernicious malarial fever (e-a. parasite), two attacks, duration of first, thirteen days. Second attack, after interim of eight days, terminated fatally at end of a week. A few purpuric spots observed. Coma twelve hours, death.

W. B. (Case III) served through the early campaign in the Philippines without illness. Upon re-enlisting he came to Cuba and was immediately taken ill with malarial fever.

It will be seen that all of the fatal cases developed coma and that Cases II and III were distinctly hemorrhagic, Case II being a well-marked instance of cerebral hemorrhage.

When we consider the death rate of this series, *less than one-fourth of one percent. of all cases*, and remember that these cases were all cases of West Indian malarial fever, reputed, worldwide, to be peculiarly pernicious, we are convinced more forcibly than ever before of the inaccuracy of the statistics relating to malarial fevers in every city of the United States. In truth this reflects

more discreditably upon the diagnostic acumen of our physicians than upon their ability as practitioners and we may reasonably expect to see a wonderful decrease in the total number of malarial fever cases reported, and of deaths from malaria, in future public vital statistics, as the scientific method of diagnosis in malaria, by the microscope, becomes popular.

Treatment.—The observation of a large number of cases has brought home to me certain convictions. First of all, I am convinced that quinine is a specific in the treatment of malarial fevers of all kinds. This statement may seem to be out of harmony with some of my expressions in the foregoing pages but in reality it is not so. I have stated and shown by charts that certain fevers, undoubtedly uncomplicated malarial fevers, withstand for a long time, very heavy doses of quinine. But I have not intimated, I believe, that these cases were not ameliorated, kept within control and eventually cured by the drug. That many more than four deaths would have occurred in the 1900 cases referred to, without the heroic use of quinine, I am morally certain. The fact that some of these cases were able to take, without perceptible ill-effect, as much as 1000 grains of quinine in a short time, and that they eventually recovered, and the fact that for one case which persists for a time in spite of quinine, twenty, perhaps, will be immediately cured, constitute, for me, evidence entirely convincing, as to the practical specificity of quinine.

Laveran, the discoverer of the parasite, first studied the action of quinine upon the hemameba malariæ by mixing a drop of an extremely weak solution of quinine with a drop of malarial blood and examining under the microscope. He observed that flagellate (extracorpuscular) forms of the organism promptly lost motility and apparently died. Dock, in the United States, confirmed this observation, and many subsequent studies have been carried out that strongly tend to prove that parasites are more vulnerable to the destructive action of quinine when free in the plasma, with the exception of certain gametocyte phases of malignant parasites (crescents), which resist the action of quinine for a long time, or at least are not made to disintegrate and disappear by it. It is generally

agreed by observers that the parasite within the red blood cell is protected to a certain degree, varying with its stage of development and the degree of degeneration of the red corpuscle, and that it is most easily destroyed by the drug when free in the plasma, immediately after segmentation and sporulation. The important things to know, then, are the length of time elapsing between the administration of the quinine and its presence in solution in the blood, and the exact time of the sporulation. The former naturally depends upon the method of administration, whether by mouth or needle, and if by mouth, upon the solubility of the salt used and the activity of absorption in the individual. The approximate time of sporulation of the benign parasites, tertian and quartan, is fortunately known after the first paroxysm.

I consider the method of administering a dose of quinine by the mouth, two hours before, one hour before, and during the paroxysm and a fourth dose an hour later, a rational and effective method in the regularly intermittent (benign) infections.

In infections with the malignant (estivo-autumnal) parasites rational treatment is rendered more difficult by the uncertainty of the time of sporulation of any given group, and the infrequency of infection by a single group. As has been pointed out these cases are usually cases of multiple infection and groups are probably sporulating throughout the entire twenty-four hours, and parasites sporulating are but rarely perceptible in the peripheral circulation. The indication, therefore, would appear to be to keep the patient's blood, by means of quinine, in a condition as toxic as possible to the young organisms as they escape into the plasma after sporulation. This can only be accomplished by the exhibition of quinine, at rather frequent intervals, during the entire twenty-four hours. If the case be distinctly paroxysmal we may be guided by this fact to give larger doses before and at the time of the paroxysm. I believe a frequent cause of failure is the omission of quinine exhibition during the night.

In a general way, I believe that it is well to give quinine at intervals of three hours throughout the twenty-four.

Studies to determine the strength of quinine solution in the

blood required to destroy malaria parasites have resulted variously. Based upon observations of fresh water amebas, it was predicted that a concentration of quinine of 1:5000 in the blood would inhibit ameboid movement of parasites, and by estimating the total weight of blood in the body the required amount of quinine could be foretold. The amount of blood in an individual of 130 lbs. weight was estimated to weigh 5000 grams. The required amount of quinine necessary, therefore, to make a blood solution of 1:5000 would be one gram (15.5 grains). The most certain way to secure this solution in blood was by intravenous injection, and Bacelli found by actual experiments with intravenous injections upon intractable malarial cases that the presence of one gram of quinine in solution in the blood was practically curative for all cases of malaria, his experience bearing out in a somewhat remarkable way the theoretic prediction.

The proper time to administer quinine is at a period sufficiently in advance of the sporulation of the parasites to assure the absorption of the drug into the blood and its presence there, in solution, when sporulation occurs. The particular quinine salt used will necessarily affect the dosage, the usual salts varying in alkaloidal strength from eighty-one percent. for the muriate to twenty percent. for the tannate. Few of the salts can be used for hypodermatic injections without preparation, their insolubility preventing. The sulphate is the salt most universally obtainable and may be rendered suitable for injection by the addition of one-half its weight of tartaric acid, another readily obtainable drug.

Without doubt, however, the bimuriate of quinine, soluble in its own weight of water and procurable in compressed tablets ready for immediate use, is the best preparation, requiring least labor and representing an alkaloidal value equal to that of the sulphate.

Of the numerous proposed tasteless preparations of quinine and the synthetic substitutes for it, no one of them has been sufficiently tested, in my opinion, to justify its recommendation in these pages.

The signs of absorption of quinine are well known and vary from tinnitus, and nausea, to such signs of poisoning as severe

deafness, amblyopia, and mental disturbance. Its presence in the urine may be noted within twenty or thirty minutes after intravenous injection.

Quinine may be introduced into the circulation by several routes, viz., through the digestive tract, by mouth or rectum; through the skin, by inunction or hypodermatic or intramuscular injection; and by direct injection of solutions into the veins.

Theoretically, the direct injection into the veins seems to be the most rational method, overcoming the possibility of failure of absorption when given by mouth and when thrown directly into the tissues. Practically, too, the method has proved itself to be one of great value and deserves to be more frequently resorted to. At present it is scarcely used at all, except in pernicious cases. Hereafter, when occasion permits, I shall resort to intravenous injections more frequently than in the past. I can testify, from experience in my own person, to the absence of special discomfort from an intravenous injection of bimuriate of quinine and urea which I caused to be administered to myself in 1901. A simple method is to make prominent the median basilic vein, by pressure or a bandage, and to introduce an appropriate needle directly through the skin and *into* the lumen of the vein in the direction of its course, and to slowly inject the contents of an ordinary hypodermic syringe, gradually releasing the pressure upon the vein above the point of injection. Under proper precautions, and these include the utmost care to secure asepsis and the actual introduction of the needle *within* the vein, no accident more serious than the leakage of a few drops of blood from the vein into the tissues under the skin will occur, and even this may be obviated by applying a compress over the puncture site immediately after injection. The procedure is less painful than the exposure of a vein by an incision in the integument.

For practical purposes the method of inunction administration may be disregarded.

In most cases quinine given by the mouth, in acidulated solution or capsules, will ultimately destroy the malaria parasites in the blood, providing the stomach remains tolerant.

I believe the administration of ginger, powdered, in capsules with quinine, or in syrup, added to solutions of quinine, or in the form of ginger ale, assists materially in preserving the tone and tolerance of the stomach.

In administering quinine by mouth it is well to remember that hydrochloric acid is normally secreted by the stomach, in the gastric juice, upon the introduction of food. It is therefore wise, if possible, to have sufficient food in the stomach to excite the flow of gastric juice when quinine is given, as the drug is kept in solution there by the presence of acid and is absorbed from that viscus while in solution. It is claimed that quinine given per os is only absorbed from the stomach, the alkaline reaction of the intestinal secretions interfering with its absorption beyond the pylorus.

That quinine absorption occurs from the colon or rectum is a demonstrated fact to which I have referred elsewhere. It must be regarded as a feasible route of introduction, however unpleasant it may be.

When the stomach loses its tolerance before the destruction of parasites is complete, resort should be had to hypodermatic, intramuscular, or intravenous injections.

As to dosage, I am guided by effects, always bearing in mind the points relative to time, set forth above. Microscopic and thermometric observations are better indices of the effect of quinine in malarial fevers than the subjective sensations of the patient.

In a general way, I may say that I have found two, three and five grain doses of quinine, by the mouth, insufficient in tropic malarial fevers. I prefer doses of ten, twelve or fifteen grains.

If resort must be had to the hypodermatic method certain precautions are indispensable. A complete and sterile solution, not extremely concentrated, an aseptic instrument and an aseptic technique will exclude the possibility of abscess formation. If for any reason the solution is not absorbed, necrosis of the soft tissues containing it may occur, but these pseudo-abscesses will be found not to contain pus. The bimuriate of quinine and urea,

by reason of its complete solubility, has given me the best results. Intramuscular injections have distinct advantages over simple subcutaneous ones and it is probably wiser to abandon the superficial tissues just beneath the skin as unsuitable sites for depositing solutions of quinine.

A syringe larger than the ordinary hypodermatic syringe should be used and the needle should penetrate to the deeper tissues of the back or buttock. The arm is not a favorable site for these injections. An antitoxin syringe, two-thirds full of a solution of ten grains of the bimuriate of quinine and urea, may be used. I have found this dose, repeated according to effect, about the proper one. The greatest care to secure asepsis in preparing the skin, solution, syringe, and the hands of the operator, must be observed if abscesses are to be avoided. The injections are frequently followed by pain, which sometimes persists for several hours.

Whatever route be chosen, however, the physician must be certain that absorption of the drug occurs, and the surest indications are the occurrence of ringing in the ears, or slight deafness, and the other evidences of cinchonism. If the infection with which we are confronted is a grave one (and any infection with parasites which are not benign may suddenly become grave), the foremost consideration is to secure and maintain a solution of quinine *within the patient's blood.*

It seems needless to add that the conservation of the patient's vital forces and strength by proper stimulation, nourishment and nursing, is of as great importance in malarial as in other fevers.

In few, if any, other diseases is the need for blood building as urgent and imperative as in the various forms of malarial disease. Whenever it is possible to combine hematics and constructive treatment with antiparasitic medication it should be done, even in the acute fevers of brief duration.

The various conditions of asthenia, hyperpyrexia, diarrhea, delirium, etc., should be met with appropriate treatment as they arise.

Calomel enjoys an ancient and time-honored reputation as an

adjuvant to quinine in the treatment of nearly all varieties of malarial disease and it doubtless deserves some credit when used judiciously and in response to indications, but it should be remembered that it has no specific powers and that it may be misused, and in fact it frequently is.

The use of antipyretics and analgesics, such as phenacetine and acetanilide, in various combinations, undoubtedly often adds something to the comfort of the patient suffering from malarial fever, but owing to the dehemoglobinizing properties of these drugs there is danger that they may add to the asphyxia already present and it is probably wiser to omit their use from the treatment.

Bromides and opium preparations, cautiously used for the relief of suffering and cerebral symptoms, are probably safer.

Ice, when obtainable, can be utilized for the patient's comfort if used in ice caps or in iced drinks, but its employment to reduce temperature in iced baths, other than sponge baths, is not to be advocated in a disease where one of the greatest dangers lies in hyperemia or engorgement of internal organs, such as the liver, spleen and brain, except perhaps in the event of dangerous hyperpyrexia. For malarial headaches the mustard foot bath, with an ice cap to the head or back of the neck, may be advantageously combined with quinine and bromides internally.

LABORATORY DETECTION OF MALARIA PARASITES.

The blood evidences of infection with the hemamebas of malaria are three in number, (I) the recognition of parasites in the blood; (II) the presence of pigment in the blood; (III) the leucocytic phenomena.

Descriptions of all of these evidences and frequent references to them have already been made and it is proposed to describe the methods of procedure and the technique of blood examination for these evidences here, in the order given. The ability to intelligently undertake a blood search of this character presupposes an acquaintance with the microscopic appearance of normal human blood. As normal histological studies cannot be taken

up in this work the student should have access to books of reference, a microscope and a few stains, and should familiarize himself with the appearance of human blood films, stained and unstained. There is never any difficulty in securing specimens, either from one's own blood or from his friends or co-workers, and by practice, and *only* in this way, one becomes familiar with the variety in color, shape and size of red blood cells and leucocytes, with the appearance of vacuoles, artefacts, crenations and dirt. Familiarity with the appearance of these normal variations, the changes produced by physiologic metamorphosis in blood cells, the effects of pressure between cover-glass and slide, and the accidental introduction of particles of dust or extraneous material will prevent many mistakes and render much easier the detection of pathologic organisms and changes. Simple methods will be described and the technique will be stripped of unessentials, as nearly as possible.

The procedure of *preparing films of fresh blood, unstained, for immediate examination*, will first be given.

The site to be punctured when selected, should be cleansed with alcohol, and dried. Either the ball of the finger or the lobe of the ear may be chosen. The ear presents the advantages of being more easily cleansed, less painful to puncture, and of being outside of the patient's range of vision. He is thus spared pain, fright, and the sight of blood. In examining one's own blood the finger-pad will be found most accessible. Soap and water, followed by alcohol only, should be used, antiseptics which might affect the blood drop being avoided. The needle *must* be clean and *sterile*, conditions easily secured by flaming over an alcohol or gas burner. An ordinary household sewing needle may be used but a surgeon's needle with a cutting or trocar point is preferable, puncturing the skin with less pressure and pain. Special needles for securing blood accompany most devices for blood counting and hemoglobin estimation, and may be used when available. Pressing or squeezing the tissues is apt to produce blood drops containing more leucocytes and more deformed cells than blood which flows unassisted. The first drop should be gently wiped away and the second small drop appearing should

be transferred to the cover-glass. The middle of the cover-slip (either round or square glasses may be used), should be touched to the *summit* of the blood drop upon the ear or finger so lightly that a droplet no larger than a pin head will be transferred to it. Next gently drop the cover-glass upon the middle of the slide, with the charged side down, and allow it to settle by its own weight, when the droplet of blood will spread evenly between slide and cover-glass. Nothing but practice will give facility in painlessly securing the drop of blood, deftly transferring it to the cover-glass, and mounting it upon the slide without undue pressure. Cover-glasses should be handled only with forceps. Both cover-slips and slides should be prepared before the puncture is made, conven-

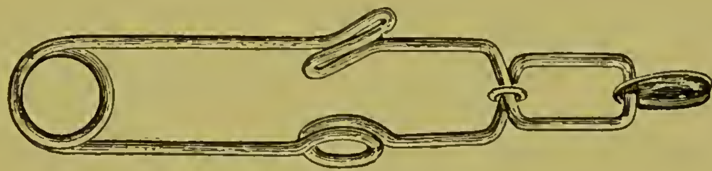


Fig. 60.—Stewart's Cover-glass Forceps.

iently placed upon a table and covered with a Petri dish or similar covering to protect from dust, flies and other contaminations.

Slides and cover-slips need not be sterilized but must be clean, dry and free from every trace of grease. They may be prepared by immersion in a three percent solution of hydrochloric acid in alcohol and wiping with a clean linen cloth just before using, or by previous cleansing with an acid solution and storing in a wide mouth bottle containing equal parts of alcohol and ether until desired. Both should be polished dry with a linen cloth before using. When the cover-slip has settled down upon the slide and the blood film is thoroughly spread the preparation is ready for immediate examination. If it be desired to postpone examination for an hour or so, or to make a protracted study of the specimen, it will be well to pencil the edges of the cover-glass with a fine hair pencil dipped in vaseline. In this way air is excluded and evaporation of the film, which causes the cover-slip

to press more firmly upon the glass slide and thus to deform the corpuscles, is avoided. Preparations thus sealed serve well for a number of hours if properly cared for. Several films at a time should be made from a single puncture. In this way one is reasonably sure of one or two good films and is prepared against accidental breakage. The importance of attention to every detail connected with the preparation of blood films is great. The end desired is to secure films in which the blood is so evenly spread that the red cells, which we particularly desire to study, will be so distributed that in a portion of each film they will appear in a single layer, with their plane surfaces upwards, discrete and evenly separated from each other and free from pressure.

Manson (p. 38) thus describes the characteristics of a successful preparation. "On holding a successful preparation up to the light, one or more areas, each made up of three zones shading into

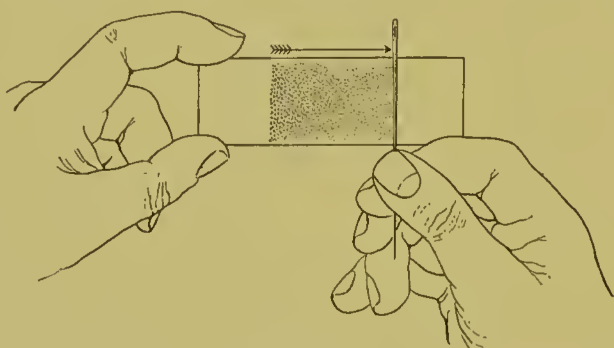


Fig. 61.

each other, can be made out with the naked eye. Each such area includes a peripheral zone of reddish tinge, a middle zone having a somewhat iridescent look, and a central zone absolutely devoid of color. Successful preparations may be recognized by the presence of these zones. Preparations not exhibiting this appearance should be rejected; it is a waste of time to examine them."

The procedure in the preparation of films for staining differs considerably from that for fresh specimens. Preparing specimens for staining involves the artificial spreading of the blood over the cover-glass to secure a thin even film which must then be dried and

"fixed" or hardened before the dye or stain is applied. A good simple method is to transfer the blood droplet, as described above, to the cover-glass and then to spread it with a straight needle (see illustration). This droplet should be transferred to a point upon the cover-glass (or slide) near its edge and a long round needle should be laid flat upon and across the cover-glass, its middle point just behind the blood drop; after an instant, in which the blood will run along the needle, it should be gently swept across the glass, spreading the blood in a thin film. If desired the spreads for staining may be made upon glass slides instead of cover-glasses in a perfectly similar manner. The straight edge of a cover-glass or slide, held at an angle with the surface on which the blood is to be spread, may take the place of a needle in spreading, the edge being drawn over the surface, spreading the blood as it moves. There are several other ways of spreading blood, as for instance between two cover-glasses, placed face to face and then slid apart, but I have found the method just described easier and productive of better films than the others. Whatever method is pursued, practice will improve one's technique and results. The films should now be dried in the air, under cover to protect from dust and hungry flies. When thoroughly dry proceed to *fix* the films. *Fixing* by heat has been generally abandoned except for a few special staining methods which require it. Flaming the film is most unsatisfactory and fixing in the hot chamber is less convenient and less satisfactory than by alcohol and ether. Immersion in absolute alcohol, or in equal parts of ether and absolute alcohol is the best method of fixing films. It is important that the alcohol be absolute and free from water. If haste is necessary it will usually be found that the films are sufficiently fixed at the end of fifteen minutes. After fixing in alcohol permit the film to drain and then to dry in the air. If heat has been used for fixation, or if the alcohol has absorbed water, small round vacuoles, due to water or air, may appear in the red corpuscles and give rise to errors. Methyl Alcohol (wood alcohol) is a constituent of one of the best known stains (Leishman's) in which method the preliminary fixing is omitted, fixation and staining being effected simultaneously in this process. Methyl

Alcohol as a preliminary fixing agent is sometimes used as a substitute for absolute alcohol, it being obtainable often when absolute alcohol is not. It is not entirely satisfactory, however. Another method commended for use when absolute alcohol is not at hand is to expose the film for two or three minutes to the vapor of formalin. Preliminary fixation is necessary to prevent the solution of the blood by watery preparations of various stains in nearly all methods. When once fixed, watery solutions will not dissolve blood films. Fixed films may be preserved for a good while before staining but in such cases should be labeled carefully. If the films be made upon glass slides the memoranda can be scratched upon one end of the film with a pin or sharp pointed instrument or traced upon the reverse side of the slide in ink. Slide films are much less fragile than cover-glass films and more easily labeled and preserved.

The relative merits of studying fresh or stained films is a much discussed question and the truth of the matter is that familiarity with both methods is highly desirable for the student who wishes to do more than to simply diagnosticate malarial disease. Only in fresh specimens can the life changes in the parasites be seen, and mistakes are certainly less apt to be made if the student actually observes motility in the parasites, and the phenomena of sporulation, exflagellation and phagocytosis. On the other hand the advantages of dry films are several. They are more easily prepared and are permanent, permitting preservation and repeated examinations of specimens months after they are taken. Certain refined methods of staining also bring out the structure of malaria parasites, particularly the youngest forms, in a manner unknown in wet films. If desirable a long list of staining methods might be given, each one possessing, in the opinion of its advocates, distinct advantages over all others. In the interests of simplicity and utility, however, only such

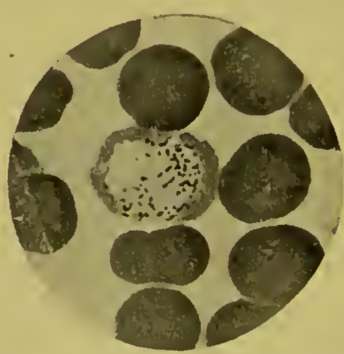


Fig. 62.—Benign tertian parasite, presporulating stage. x 1000. (From Williams' Bacteriology.)

methods as personal experience and the judgments of experienced workers in tropical diseases commend to me will be described.

Stains for malarial blood films are of two general kinds: (1) those which stain the parasite, both protoplasm and nucleus, a single color, and (2) those which impart different colors to nucleus and protoplasm.

In the first class are included the older methods whereby it was sought to stain the parasites of malaria and the leucocytes one color, leaving the red cells unstained or counterstaining with a contrasting color. This plan has much to recommend it, particularly for beginners, and several methods will be given.

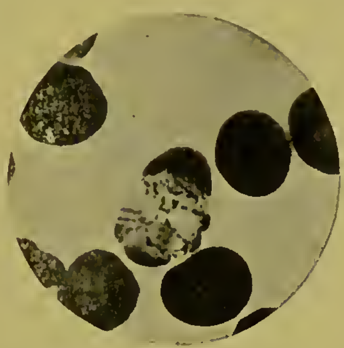


Fig. 63.—Benign tertian parasite. Sporulation. x 1000. (From Williams' Bacteriology.)

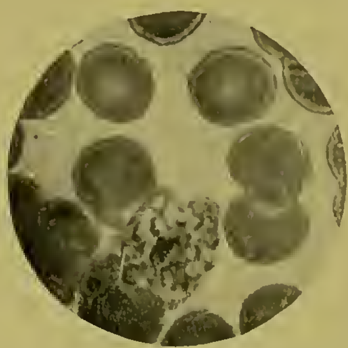


Fig. 64.–Segmentation completed. Benign tertian parasite. x 1000. (From Williams' Bacteriology.)

The first two methods described are inelegant but useful devices to assist diagnosis only. The first one is designed *to Stain Fresh Blood.*

With a six-tenth percent. salt solution make a concentrated solution of methylene blue. Place a drop of the solution upon the site from which blood is to be taken and then puncture through the drop. Mount a very small drop of the mixture upon a cover-glass and slide and examine. The leucocytes and parasites should take the blue stain.

The thick film method for rendering diagnosis easier has attained considerable favor since proposed a few years ago. A *thick* film or smear of blood is made upon a slide (or other piece of glass). This is thoroughly dried but *not fixed.* Immerse the

dried slide film in a one-half percent. solution of acetic acid in two percent. formalin solution. By the time the film is decolorized (by the dissolving out of the hemoglobin from the red cells), the film is fixed and ready to stain by any simple basic stain. Only the leucocytes and parasites will stain and the chance of discovering parasites is increased proportionately with the increased thickness of the film and the volume of blood examined. Considerable sediment is left on the glass but this does not affect the value of the method. As originally proposed this method did not include fixing, the thickness of the film and the cohesion of the corpuscles serving to keep the film from being washed from the glass. In the original method the hemoglobin was dissolved out of the red cells by water only. After draining and absorbing the water with bibulous paper a simple methylene blue stain was applied and the smear was rewashed, dried and examined. *Formula for decolorizing and fixing solution for thick films:* Acetic acid $\frac{1}{2}$ gram, formalin 2 grams, water to make 100 c.c.

The Borax-methylene-blue Method is a satisfactory single stain method of the first class mentioned, staining nucleus and protoplasm alike. Biborate of soda (borax) 5 grams, methylene blue (medicinal or Grubler's) 2 grams, distilled water to make 100 c.c. Spread a few drops over the fixed film to be stained. After one-half minute wash well under a tap of running water. Dry well with filter paper. Next mount in balsam for examination, if the film is upon a cover-glass, or examine without mounting if the film is upon a glass slide, placing the drop of cedar oil for the immersion lens directly upon the stained film. There is danger of overstaining by this method and it is sometimes necessary to dilute the staining solution with an equal amount of water. It is, however, a quick and reliable stain. Like other methylene blue stains it is improved by age.

Double Staining—Two Solution Process. A method of the first variety, omitted from the latest editions of works upon tropic diseases, which has, nevertheless, served me long and well, is the double staining process whereby the film is treated with two different stains, an eosin solution to stain the red cells and a

methylene blue solution, subsequently applied, to stain the leucocytes and malaria parasites. The procedure is as follows: Subject the fixed blood film for two minutes, more or less, to the action of a half percent. solution of eosin in seventy-five percent. alcohol. Wash thoroughly in running water and dry with filter paper. This process tints the erythrocytes and the eosinophile leucocytes pink, the shade depending upon the activity of the stain and the time of exposure. Next expose the film for a minute to the action of a concentrated aqueous solution of methylene blue. The borax methylene blue stain described above serves well, an exposure of thirty seconds only being required. Wash thoroughly in running water, dry with filter paper, mount and examine. The second solution stains malaria parasites and leucocytes blue in contrast to the pink stained red corpuscles. The time of exposure to both staining solutions may be varied according to the shades of staining desired. There is no differentiation between protoplasm and nucleus in this process but it admits of nice modulations in two color effects and constitutes a useful method. With determined data as to the activity of solutions and the time of exposure required, and strict adherence to careful timing and thorough washing, this method should give constant and satisfactory results.

Fig. 65.—Crescent. (Gametocyte.) Estivo-autumnal parasite. x 1000. (From Williams' Bacteriology.)

Of the other class of stains mentioned above, (2) *those which impart different colors to nucleus and protoplasm*, two examples will be given. Of one of these Stephens and Christopher (The Practical Study of Malaria, p. 9) speak as follows: "There is one stain, however, so much more strikingly effective and generally satisfactory than other stains, that for routine use no alternative methods need be considered. This stain is *Romanowsky's* chromatin stain." Chromatin, it should be understood, is a constituent of nuclei with an affinity for a certain red stain which is developed by the mixing, under special conditions, of eosin and

methylene blue. All of the methods for differentiating nuclei and protoplasm depend upon the development of the red stain and all are practically modifications of the Romanowsky method which will be described. The highest grades of eosin and methylene blue are essential to making this stain. Heat is necessary to develop the red body in the methylene blue solution.

Romanowsky Method. To a half percent solution of sodium bicarbonate add one percent. of methylene blue (Grubler's). Steam in a steam sterilizer for one hour. This develops the desired red principle and the solution is now "polychrome" and ready for use when cooled, without filtering. The second solution is one of eosin, 1 part to 1000 parts of water. These two solutions are now used as stock solutions and before use for staining are diluted with water, 5 parts being taken with water enough to make 100 parts of staining solution. Now mix equal parts of the staining solutions (about 1 c.c. of each) and pour on the films to be stained. Leave the stain upon the films for from ten to thirty minutes or even longer. Wash in running water and dry with filter paper. If the red corpuscles show a blue tint wash again in water. If soaked in water long enough the stain will entirely disappear. The film can be stained again, however. A moderately stained specimen brings out the details best.

The other stain, *Leishman's*, is produced by the interaction of eosin and the polychrome methylene blue of the first described method. The product is the filtrate from a mixture of the solutions of polychrome methylene blue and eosin. It is prepared as follows: Place 100 c.c. of the polychrome methylene blue in a shallow dish. Gradually add the 1 to 1000 solution of eosin until a film forms and the eosin color shows in the fluid.

It will require about four times as much eosin solution as methylene blue solution to develop this film and color. Thoroughly mix by stirring with a glass rod and expose for a number of hours to the air, stirring from time to time. Next filter the mixture. The stain is in the filtrate and must be washed with distilled water until the washings are almost free from the blue color.

DESCRIPTION OF COLORED PLATE.

(Reproduced, by kind permission, from Greene's Medical Diagnosis.)

Hemameba malariæ of three varieties. Stained by Wright's stain.

THE QUARTAN PARASITE (BENIGN).

1. Young hyaline form. 2, 3, 4. Rings showing chromatin borders (red), and pigment granules.

5, 6. Full grown parasite intracellular and extracellular.

7, 8, 9. Presegmenting forms and segmentation.

10. Spherical gametocyte. 11. Normal red blood cell.

12. Flagellate gametocyte.

THE TERTIAN PARASITE (BENIGN).

13 to 20 inclusive illustrate the intracellular growth of the parasite. 21. Segmentation. 22. Flagellate gametocyte.

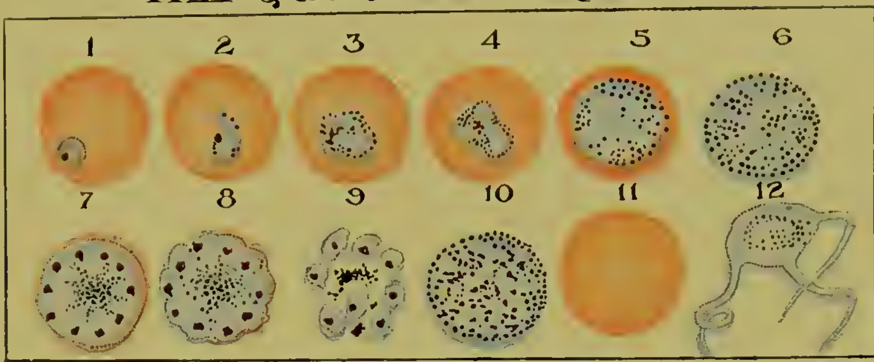
THE ÆSTIVO-AUTUMNAL PARASITE.

23 to 27 inclusive illustrates growth of intracellular parasite, 25 and 26 being double infections.

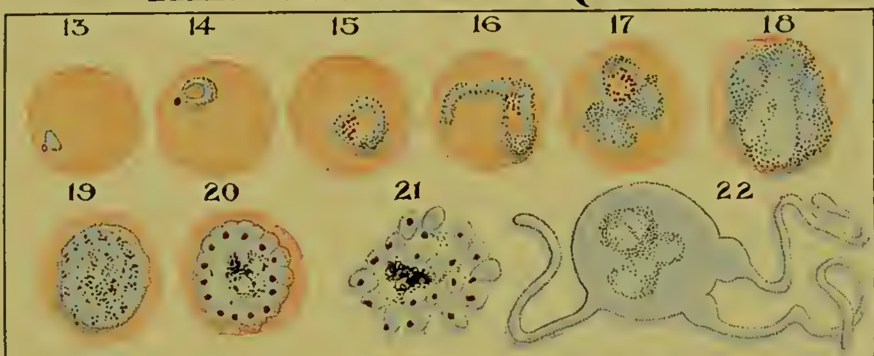
29, 30, 31. Full grown parasite, presegmenting, segmenting and extracellular, *rarely* observed in peripheral blood.

32, 33, 34, 35, 36, 37. Crescent, ovoid and spherical gametocytes and flagellated gametocytes.

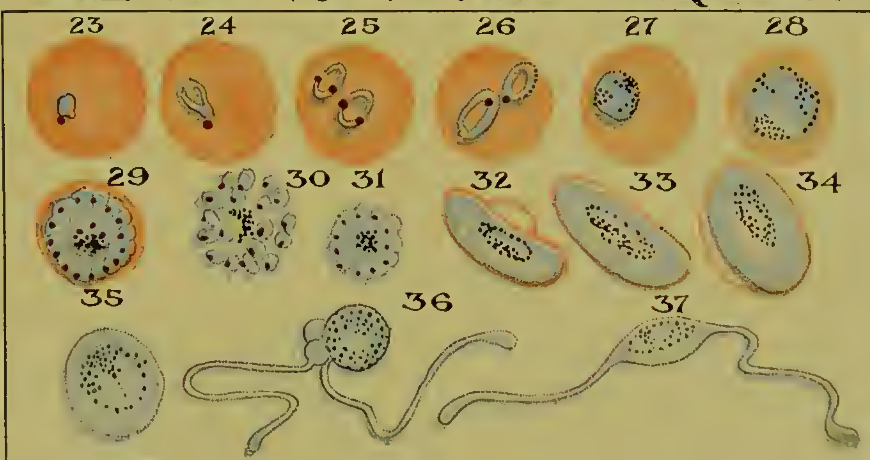
THE QUARTAN PARASITE



THE TERTIAN PARASITE



THE ÆSTIVO-AUTUMNAL PARASITE



Next dry thoroughly and pulverize finely. This product is the *Leishman* stain. It may be obtained ready made in powder or in tablet form. For use it is dissolved in methyl alcohol and applied to unfixed films, the methyl alcohol acting as the fixative. A 0.15 percent. solution of the stain in methyl alcohol is the strength ordinarily used. Drop a few drops upon the films to be stained and after one-half to one minute, during which the fixation occurs, add twice as much distilled water and mix upon the slide. After five minutes wash well in distilled water and then permit a few drops of distilled water to rest upon the stained film for a minute or more. This clears the specimen, dissolving out the excess of blue in the stain and is an essential step in the process.

After clearing wash again in distilled water, drain and dry without heat, and mount.

Wright's stain is applied in a similar manner to Leishman's and gives beautiful results (see colored plate), the erythrocytes appearing pink or orange; the protoplasm of the parasites is light blue; the nuclei of the young hyaline parasite appears as a single red spot. As the parasite increases in age and size the red spots become more numerous and in the presegmenting or segmenting stage each spore presents a distinct red nucleus. Pigment granules are unstained, appearing as black dots. The preparation of Wright's stain is somewhat complicated.

The Romanowsky stained parasite presents a distinct blue ring, either light or dark in shade, and a light red dot representing the nucleus (chromatin) near the margin of the blue ring. Pigment remains unstained.

Stained by the Romanowsky method the erythrocyte appears of a faint green hue. With the Leishman stain it appears faintly pink and with the Wright stain it appears orange or pink. In essential respects, however, the appearances of the stained parasites, when treated by Romanowsky's, Leishman's or Wright's method, are very similar.

Stephens and Christopher lay down a rule that no small body should be pronounced a parasite (when stained by the Romanowsky method) unless three distinct parts are apparent; a red

nucleus, a blue protoplasm and a vacuolic area within the ring (undistinguishable in irregular forms).

Gametocytes, whether crescent, ovoid or spherical in shape, stain definitely and unmistakably, showing central pigment, clear outlines, and generally a red central portion, dotted and surrounded by pigment granules.

A red stippling of the erythrocyte with fine granules of bright color is observed in cells invaded by the benign tertian parasite, when the Romanowsky stain is used. These red spots are known as Schüffner's dots and the appearance is considered to be of diagnostic value.

Concerning the actual appearance of the *unstained* parasite in fresh blood, the following statements may be made, by way of review.

Young intracorpuscular parasites are small pale discs or rings of somewhat irregular outline, of the appearance of ground glass, showing at first no pigment nor ameboid activity. Later pigment and motility become apparent and help to differentiate the parasite from crenations and vacuoles. Both vacuoles and crenation effects, when focused upon, develop indefinite outlines while the parasite appears clearly defined in outline.

A blood platelet resting upon a red cell may also resemble a hyaline parasite but lacks its opacity.

The older forms of the parasite should be recognized from the descriptions and illustrations but it is difficult to depict the color and appearance of the young hyaline parasite. Familiarity with this appearance will come with practical experience.

A melaniferous (pigmented) leucocyte presents no great difficulty to recognition, either in the stained or fresh state, and is of diagnostic import. The large mononuclears are the leucocytes generally found pigmented. The pigment is both black and yellowish-brown and appears in granules within the colorless protoplasm of the leucocyte. Pigment in the blood plasma is also occasionally seen.

CHAPTER VIII.

MALTA OR UNDULANT FEVER.

Synonyms. Mediterranean Fever; Gibraltar Fever; Rock Fever; Cretan Fever; Neapolitan Fever; Cyprus Fever; Levant Fever.

Definition. This disease is an endemic, specific, febrile disease of man, somewhat tropical in its distribution, and of long and indefinite duration. It is characterized by a pronounced tendency to relapse and its principal clinical manifestations are anemia, constipation, sweating, arthralgia with joint swelling, and an undulating temperature curve. In view of this curve the name undulant fever was proposed by Hughes. The disease is infectious and inoculable and is due to the presence in the human body of the *Micrococcus Melitensis*, discovered by Bruce in 1886 and named by him after the island of Malta. The disease does not appear to be contagious and the mortality is not high, as compared with enteric fever. Bruce found it to be about two percent.

Facts of History and Geography. The ancient history of Malta fever is entirely too obscure to warrant us in making any definite statements concerning it. Although doubtless observed and described repeatedly, it was usually confused with malarial and typhoid fevers. Only since its definite classification as a distinct febrile disease of known causation, and the discovery of a definite diagnostic measure, has it been studied systematically. Generally speaking, it is endemic in many of the countries bordering on the Mediterranean Sea and it has its principal home in these subtropic countries and islands. In Italy, Sicily, Sardinia, Malta, Turkey (Constantinople), Algiers, Tunis, and Gibraltar the disease is continually present in endemic form. The Red Sea Coast, Zanzibar, Africa, India, Porto Rico, Cuba, Venezuela and Uruguay, South America, the Philippine Islands,

England and the United States have all presented cases, usually sporadic ones, in which no histories of Mediterranean travel or communication could be elicited. It is definitely proven that the disease has a widespread distribution, heretofore unsuspected, along tropic and subtropic sea coasts and river banks. During the last twenty years the disease has decreased ninety percent. at Gibraltar, its former home, and by some observers this decrease has been ascribed to improvements in drainage and sanitary conditions in and about the great rock. The earlier studies were chiefly made from British soldiers garrisoned at Malta and Gibraltar. Its seasonal prevalence there was greatest from June to September, and least from December to February. Since the Spanish-American war in 1898 quite a number of cases have been encountered by United States Army medical officers in Porto Rico and the Philippine Islands and by civil practitioners in the United States. Assistant Surgeons Cox, Chamberlain, Curry, Craig and Strong and Drs. Musser and Sailer of Philadelphia have added to our knowledge of this disease.

The observations of Cox in Porto Rico, and of Curry in Manila, P. I., concerning the occurrence of Malta fever in these two American insular possessions, as reported in the annual reports of the Surgeon-General of the Army for 1899 and 1900, are interesting.

The report of Lieutenant Cox is as follows. (Surgeon-General's report for 1899, p. 286.)

"*Case of Malta fever, reported by Lieutenant Walter Cox, assistant surgeon, United States Army, San Juan, Porto Rico, July* 14, 1899. On arriving in the general hospital at San Juan in February of this year, my attention was attracted to the peculiar temperature curves shown by some of the fever cases in the hospital, and on being put in charge of the clinical examination of the blood, etc., I soon found that we should probably have to look to other explanations than malaria and typhoid for a satisfactory cause in explaining them. Having read Dr. Musser's interesting report, in the Philadelphia Medical Journal for December, of a case diagnosed by him as Malta fever in an officer who contracted

his disease in Porto Rico, I lost no time in the attempt to find whether any of our cases might also be due to similar infection, and in this connection would like to bring to your attention one in particular which seems to me to support Dr. Musser's conclusion that this island may be an endemic focus of this disease.

"The patient was a private of the hospital corps, thirty years of age, who was admitted to the hospital January 14, 1899, with a fever diagnosed as remittent malarial. He had been well during his service in the campaign and at Guayama, but had some trouble and was tried by court-martial and sentenced to a three months' term in the guardhouse of the old Spanish barracks, a place he described as, at that time, terribly foul and damp. Here he contracted his fever. He was in the guardhouse from December 25, 1898, to January 14, 1899, the fever commencing January 11. On admission he complained of pain all through his body, especially in his bones and joints. He had two chills on successive days when first taken; none afterwards. He felt ill and stupid. His appetite was poor and he slept poorly. Bowels at first loose, but later constipated. No urinary disturbance. The temperature continued with marked daily remissions, on some days as much as 3°, till he came under my observation, February 10, when he was noted at once as an unusual case. The temperature came to normal gradually, being normal in the morning and 101° or 102° in the evening, and beginning February 27 he had several days of apyrexia. Then a gradual rise came on, and on March 15 his fever reached 104°, again coming to normal March 27. He was discharged from the hospital on April 3, having had six days of apyrexia, but was re-admitted April 7 with another recrudescence, the temperature being 102°. His fever fell to normal in several days. He was discharged from the Army April 15 and left for home two weeks later. I saw him just before he left, he said he had had one or two feverish evenings after discharge.

"Here, then, was a low fever lasting from January 14 to April 15 (ninety-one days) and showing the typical undulatory character and marked daily remissions which were noted by Dr. Musser.

Repeated tests for the malarial organism were made by me and nothing suspicious found. Quinine had no effect on the temperature. The Widal reaction with a delicate organism, tested in other cases typically typhoid, was entirely negative, there being no reaction even with low dilutions. Through the kindness of Dr. Welch, of the Johns Hopkins, I was enabled to obtain a culture of the micrococcus melitensis of Bruce, and on testing the blood there was marked agglutination in dilutions as high as 1 to 60 in twenty-five minutes. The dilution of 10 and 1 to 20 showed marked reaction in five minutes. Normal serum and the blood of a typhoid patient produced no visible effect on the organism. It is evident, therefore, that clinically, and also by the serum test, this case supports the view that Malta fever may be endemic here; and the fact that there were so many cases, in this hospital, of fever certainly not typhoid, in which the malarial organism was not demonstrated and on which the administration of quinine had no effect, makes it probable that many more cases might have been proven to belong to this type."

Dr. Curry's report from Manila (Report of the Surgeon-General, United States Army, for 1900, p. 227) indicates an equally interesting state of affairs in that city and is reproduced below. Both reports emphasize the suspicion that "place infection" may be one of the characteristics of this disease. In both Porto Rico and the Philippine Islands old Spanish buildings were, of necessity, occupied for various purposes, as barracks, hospitals, prisons, and officers' quarters, during the early days of occupation by American troops.

The accidental inoculation of Dr. Strong, related by Dr. Curry, is an example of laboratory infection, to which I have already referred. A similar case occurred in the army laboratory at Washington within the past three years, the victim in this case being a student medical officer in the Army Medical School. Dr. Curry's report is as follows:

"1. Some time ago Dr. Strong, the pathologist, performed an autopsy on a man who had died after a continued fever of long duration. Postmortem examination was negative as to typhoid

and to malarial fever. From the cultures of this case was obtained an organism identical with the coccus melitensis (the causative agent of Malta fever). This organism was inoculated into monkeys and produced the typical symptoms of Malta fever. Autopsy on the animals inoculated showed typical lesions, with the development of the same coccus, which in turn produced the same disease in other animals. Dr. Strong in some manner inoculated himself during these investigations, and has now Malta fever.

"2. At a postmortem examination on a case received from the Second Reserve hospital December 27, 1899, a similar condition was met with as in Dr. Strong's case—i.e., no typhoid, malaria, or other recognized pathological condition. Cultures from this case showed the coccus melitensis.

"3. A case of continued fever in the officer's ward of the hospital, whose blood was negative repeatedly to malaria and typhoid, gave the reaction with the melitensis.

"4. A case on the hospital ship *Relief*, whose blood gave negative results as above, also reacted with the melitensis.

"As the results of the investigations of Dr. Strong, showing the first case to be one of undoubted Malta fever, the second case being also one of undoubted Malta fever, and the positive results of the blood serum reaction of the third and fourth cases, we have evidence that Malta fever prevails here to a considerable extent. It is probable that many of those cases of continued fever which fail to react to Widal's test for typhoid, and which are negative to malaria, are cases of Malta fever. There are a number of such cases in the hospital at the present time, and no doubt the same is true of the other hospitals."

Etiology and Prophylaxis. Concerning the cause of this disease, which seems to attack young adults by preference, it has already been stated that *micrococcus melitensis* plays the specific rôle. While the method of its transmission is entirely unsettled as yet, and the question whether the organism is air borne or water borne, or both, is an open one, it has been shown to be inoculable, and thus productive of the disease, and the typical manifestations of the disease have been experimentally and acci-

dentally produced in both man and monkeys. Under the section on Laboratory Detection the morphology and cultural characteristics of micrococcus melitensis are dealt with and a general description of the organism is given.

It has been demonstrated in profusion in blood drawn from the spleen by means of a hypodermic needle in life (Bruce), and it is found in the splenic pulp after death.

English writers seem to agree rather generally that filth and unsanitary conditions favor, and play some part in the production of Malta fever, but there is no conclusive evidence that this is true, however likely it may seem.

On account of our ignorance concerning the method of transmission to human beings of *micrococcus melitensis*, our *Prophylactic* efforts cannot be very specific. In the light of our knowledge that the disease is inoculable we are justified in demanding the destruction, or exclusion, of all mosquitos or other insects wherever cases of undulant fever occur. On general principles, too, we should disinfect all excreta from patients with this disease and provide a supply of pure sterile water for drinking purposes. Travelers should avoid visiting places in which the disease is endemic, especially the Mediterranean cities and countries, during the hot months.

In the Lane lectures on Tropical Diseases delivered by Sir Patrick Manson, at San Francisco, in August 1905, attention was called to recent reports of the commissioners of the Royal Society, who have been studying undulant fever in the island of Malta, concerning the infection of goats with micrococcus melitensis. They have shown that a large proportion of the goats in Malta are infected with the organism and that the milk of these goats contains the micrococcus. As the sole milk supply of the inhabitants is obtained from goats the possibility of conveyance of undulant fever, long prevalent here, is suggested. A most natural and rational prophylactic procedure, therefore, in Malta and in other places where similar conditions abound, would be to discontinue the use of goats' milk which has not been sterilized by boiling. Concerning this work in Malta, Barker, in the Journal

of the American Medical Association for June 16, 1906, writes as follows:

"Some very important work has been done during 1905 by the so-called Mediterranean Fever Commission, consisting of Colonel Bruce, Major Horrocks, and Drs. Shaw, Zammit and Johnstone. It is regarded by some as the best piece of work of the year in tropical medicine. This commission studied the duration of life of the causative micrococcus outside of the body, and made investigations concerning its occurrence in the blood, urine, feces and sweat of patients suffering from the disease; they also studied the disease experimentally in monkeys. It appears that the milk supply of Malta is derived chiefly from goats, and in June of last year Zammit made the important discovery that the Maltese goats are infected with M. melitensis; the coccus was isolated from the milk and from the urine of these animals."

Pathology and Diagnosis. In view of the low mortality rate of Malta fever, opportunities for postmortem study of its pathology are infrequent, and up to the present time there exists some difference of opinion as to the occurrence of enteric lesions. The weight of opinion seems to be against the constant, or distinctive, occurrence of lesions of the intestinal coats or mesenteric glands. The duodenal portion of the small intestine has been found congested, and the mesenteric glands have been swollen in some cases, but these seem to be coincidental findings, and by no means constant. Le Dantec states that the only constant lesion observed postmortem, in victims of undulant fever, is an enlargement of the spleen. All observers agree that the spleen is constantly and decidedly enlarged and this symptom is observed in life, accompanied by tenderness. Postmortem, the pulp is soft, dark and friable. In the other organs, cloudy swelling is apt to be observed. The liver is not uncommonly enlarged and congested and the kidneys may be hyperemic. The lungs may show congestion, bronchitis being a fairly common accompaniment of the disease.

The **diagnosis of** Malta fever is important and often difficult. Direct diagnosis from symptoms and history involves the dis-

crimination and exclusion of a number of diseases. These are enteric fever, rheumatic fever, malarial disease, tuberculosis, syphilis, suppurative fevers generally, and hepatic abscess in particular. Generally speaking, the duration and the undulant character of the fever, the neuralgic and rheumatoid pains, the profuse perspiration and the history of residence or travel in districts where the disease is known to be endemic, serve to establish a strong presumption of Malta fever. Typhoid fever can be excluded by the absence of rose spots, the typical fever curve, tongue and stools, and the absence of response to the Widal serum test. Rheumatism should not present great diagnostic difficulty, the articular pain and swelling and the profuse sweats being the only similar symptoms. Malarial disease may be diagnosed by the microscopic test, the therapeutic test and the test of periodicity. Tuberculosis should be evident from physical signs and sputum examination, and syphilis, except in its joint manifestations and the occasional occurrence of syphilitic fever, never closely resembles undulant fever. Fever due to concealed collections of pus and to hepatic abscess simulates the intermittent stage of undulant fever, but careful and thorough diagnosis, including hepatic puncture if necessary, should serve to clear up any question. In splenic puncture or aspiration, with hypodermic needle, for securing micrococcus melitensis for culture, we have a definite diagnostic test, but the procedure is not justified on account of its dangers. In the agglutination test, however, we have a valuable diagnostic method. This test is described at the end of the chapter and is applicable whenever dependable test cultures of micrococcus melitensis are obtainable. Manson, in his Lane lectures at San Francisco, related an unfortunate experience with this test, but admits its value when reliable cultures of the organism are obtainable. American experiences with the test have generally been satisfactory. Certainty as to the culture used and knowledge on the part of the observer making the test, are essential. Theoretically and practically the test is a valuable one, providing the essential conditions, of skill and reliable test cultures, are complied with.

Symptoms and Treatment. The incubation period for Malta fever is not definitely determined and is said to vary from several days to as many weeks. The disease is frequently observed in England, as an importation, in the persons of soldiers returned from Mediterranean stations, or travelers returned from countries where the disease abounds. As the time required for the journey is usually five days, or longer, it is doubtful whether the incubation period is ever less than a week. A prodromal period is rather constantly observed, extending over a number of days and marked by lassitude, loss of appetite, indigestion and headache. The tongue is coated and remains so, showing, in most cases a red tip. It does not, however, take on the true typhoidal aspect. Constipation is the rule from the onset, but diarrhea, or even bloody stools, may be observed. No rose spots occur, in contrast with enteric fever, and this fact is of diagnostic value. The fever curve is characteristic. True febrile undulations are observed and the first febrile wave varies from two to three or four weeks in length. The undulations are separated by short periods of apyrexia. These afebrile periods vary from four days to a week in length. This sequence of long febrile periods separated by short afebrile ones is considered distinctive of undulant fever. The number of febrile periods varies from two or three to six or seven, but usually does not exceed three. The second, third and later periods of fever are less extended than the first one and tend to grow shorter in succeeding periods. The temperature range is also lower. During the first fever period the daily mercury range may be as great as four Fahrenheit degrees, the maximum being 104° F., or less, and the minimum averaging about 100° F. Towards the latter part of the period the daily minimum may be 98.6° F. or less, so that the fever becomes, in reality, an intermittent of quotidian type. The maximum temperature is usually an afternoon or evening one and the minimum mark occurs in the early morning. Profuse perspiration, occurring generally at night or when the temperature is declining, is so marked a feature of this disease that it has led to the use of the term "fiévre sudorale" by French physicians. Rigors are not common.

Malta or Undulant Fever (incomplete.)
Showing two febrile periods and one apyretic period.
Chart of an average case would be about twice as long as this specimen chart.

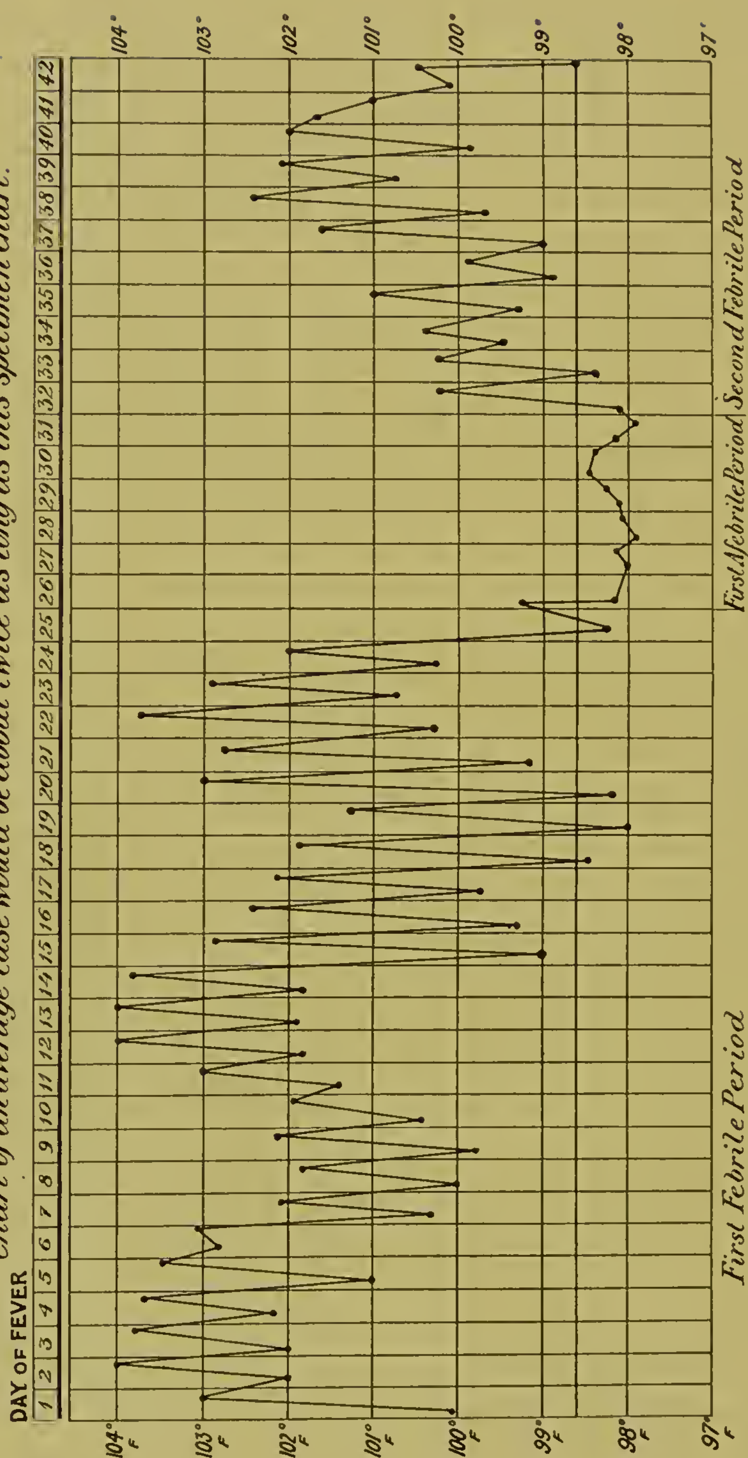


Fig. 66.

When the intermittent type of fever develops it closely resembles the "hectic" fever of tuberculosis or suppuration.

While the average stay in hospital of Malta fever patients is from seventy to ninety days, the fever may last six months, and the convalescence therefrom may require eighteen months or two years.

Anemia and debility are symptoms of Malta fever, the blood showing a destruction of red cells and decreased hemoglobin value, while hemic murmurs may be heard in some cases. The pulse rate does not correspond closely with the temperature, the rate being low, unless exhaustion is a marked feature. Hemorrhages from the nose and lungs and purpuric manifestations have been noted in some cases. The possibility of enteritis and bronchitis occurring during an attack of undulant fever has already been mentioned. Pneumonia and pleurisy have also been known to occur. Transient albuminuria is occasionally noted. Symptoms referable to the nervous system are headache, delirium, insomnia, apathy, neuralgia and neuritis. The first of these, headache, is common, occurring early in the disease and persisting. It is usually frontal. The apathetic condition of mind is noted in moderately severe cases, and insomnia or delirium may be present according to the degree of hyperemia or toxemia of the cerebral nervous system. Neuralgia or neuritis of almost any nerve trunk may occur but the sciatic nerve is most commonly affected. Rheumatic, or at least rheumatoid joint or tendon involvement is very common in Malta fever; so much so, in fact, that the disease is often mistaken for rheumatic fever. Swelling and tenderness are present in the affected joints, which become inflamed in a few hours and as rapidly resolve, the same symptoms appearing in numerous joints in rapid succession. These rheumatoid joint inflammations are very distinctive and rather constant in occurrence. Moreover, they are apt to become chronic in convalescent subjects of Malta fever. Occasionally joint effusions occur.

Deviations and departures from the type of fever just described are apparently no less common in undulant fever than in enteric fever and other well known specific infections with distinctive

courses. These deviations may take the forms of malignancy or benignity, giving us fulminant fatal cases marked by hyperpyrexia, or mild, brief cases marked by trifling discomfort and debility. It will be unnecessary to describe either of these types. Undulant, continued, intermittent and mixed types are described by various writers. In the course of an apparently benign case hyperpyrexia and death may occur, a possibility to be borne in mind by the physician.

Undulant fever terminates by lysis, with the tendency to chronicity and relapse already described. Among the complications and sequellæ are endocarditis, orchitis, and, more rarely, mastitis.

No scheme of **treatment** in any sense specific or curative has been discovered or proposed for undulant fever. Neither have there been any serious suggestions of serum-therapy and there seems to be no immediate promise of developments along the lines of rational or specific curative therapeutics. The disease is necessarily a long and tedious one and cannot be aborted or cut short by any drug or drugs. It is necessarily attended with more or less exhaustion and anemia, and for this reason medicines which may depress or contribute in any way to the anemia should be avoided. Our efforts must be directed towards the control of dangerous symptoms and the maintenance of the patient's strength and comfort. The symptoms most apt to demand treatment are the fever and the rheumatoid and neuralgic pains. The former practice of administering antipyretic drugs throughout the course of the disease, and of enforcing a low and greatly restricted diet, has properly fallen into disfavor, as it doubtless contributes to the asthenia and anemia. Antipyrin, phenacetin, quinine and sodium salicylate should not be given throughout the disease and some of them should not be given at all. Quinine, although less productive of anemia than some of the coal-tar derivative drugs, has no place in the treatment of undulant fevers and antipyrin is decidedly too depressant. Sodium salicylate, for the rheumatoid pains, may be used advantageously for brief periods but is inferior to opium. Hydrotherapeutics should be given preference over drugs for the control of fever and the cold

bath and cold pack, at temperatures of 68° F., may be employed when the fever reaches 104° F. (40° C.). If this plan of treatment is followed, alcohol will not be needed, or at least not before the disease is well advanced. When cold baths are given, however, the patient should be guarded from shock by the administration, immediately before and after the bath, of half an ounce of good sherry or whiskey. If at any time cardiac weakness develops, or if the fever, or the profuse sweating, produces great prostration, alcohol should be given in small doses at regular intervals of three or four hours. The drug treatment should consist of an initial laxative dose of calomel or castor oil and little else unless the symptoms specially indicate the temporary use of an antipyretic, or a drug for the relief of pain or insomnia, or the use of a cardiac stimulant. Complications, be it understood, should be treated symptomatically as they arise. Of the greatest importance is skilled nursing and the judicious administration of a nourishing diet. During the periods of high fever, when digestion is disordered and in abeyance, substantial foods, requiring digestive efforts will be improper, and little besides milk, beef tea, chicken broth and junket should be given; but when the temperature is low semisolid foods may be given, and indeed, are often better borne than the liquid foods. Pure water should be given generously and lemonade and fresh vegetables (for their antiscorbutic properties) should be frequently prescribed. The feeding should be done regularly and frequently. If constipation or diarrhea are troublesome, an occasional laxative dose, or a small daily dose (℥ij), of castor oil may correct the trouble. When convalescence is begun, iron should be prescribed and an ample nutritious diet should be ordered. A sea voyage may hasten convalescence, and removal to a mild bracing climate is desirable, avoiding those places where dampness and cold prevail.

LABORATORY DETECTION OF MICROCOCCUS MELITENSIS.

The specific cause of Malta, Mediterranean or undulant fever is an oval micrococcus, varying from .3 of a micron to .5 of a

micron in diameter and occurring singly, in pairs, or in short chains. It is aërobic and nonmotile, although flagellæ (from one to four) have been described by some observers.

It stains with the ordinary aniline dyes and especially well with a watery gentian-violet solution. Gram's iodine method decolorizes it. It grows slowly in various media, including gelatine and agar, and in peptone bouillon. The body heat (37° C.) is a favorable temperature for cultivation but an incubator hastens its growth. It does not liquefy gelatine and growth upon this medium is feeble. In bouillon the medium becomes cloudy but no pellicle is formed; a sediment occurring later. The organism has been known to live for three weeks in milk and for three days in ordinary hydrant water and it has been shown to live for sixty days in dust and even longer in dried clothing. In sea water it dies at once but it has been observed to live in urine for from three to six days. Cultures maintained at 22° C. have remained alive for fourteen months. Exposure to the sun kills the organism at once. On agar slants, clear or white, pale colonies appear in about three days and these become milky or pearly with age.

After some weeks the surface colonies grow together in rosette forms and take on a yellow cast. The organism does not grow visibly on potatoes. Micrococcus melitensis has been isolated from human urine and blood and from the splenic pulp but it has not been recovered from sputum, feces, perspiration, or exhaled air. Feeding experiments with monkeys have been negative as to results but the disease may be produced in these animals by inoculation. There are on record a number of cases of human, accidental inoculation infection from pure cultures, which have occurred in the laboratory. Although the organism is rarely encountered in the peripheral circulation there is present in the blood serum of patients with Malta fever, an agglutinating principle for cultures of the micrococcus melitensis. Dead cultures also give the reaction, it is claimed. As motility is not a characteristic of the organism, the loss of motility, an important part of the serum reaction for *bacillus typhosus*, does not enter into this test. The agglutinating phenomenon, however, is of

great value in a diagnostic way. It is present as early as the end of the first week and persists for some years after the disease.

An easy and fairly satisfactory method of performing the agglutination test is as follows: The necessary implements are two platinum-wire loops, a glass slide and a microscope. Place upon the center of the glass slide a loopful of blood serum from the suspected patient and in a circle around this drop place ten loopfuls of bouillon. With the platinum wire loop gently unite the drops so that an admixture will take place. This represents a dilution of one to ten. To secure a higher dilution, let us say of one to forty, which is about the proper one for this organism, a loop one quarter of the size of that used for the bouillon may be used for the blood serum. To this add a loopful of a living bouillon culture of the organism, of the same size as the drop of serum. A hanging drop preparation of this admixture may next be prepared and the agglutination may be observed under the microscope.

At the same time a control experiment with normal blood serum from a healthy person should be performed. This method may be modified by using normal salt solution in place of bouillon for diluting. The method just described has often been used by me in the typhoid serum test (with various dilutions) with satisfactory results.

A certain nice judgment is required in securing accurate dilutions but this skill comes with experience. The naked-eye evidence of this reaction is observed by performing the dilution of the serum and the inoculation with the culture in a narrow, vertical tube. This tube remains in a vertical position and is placed in an incubator. Turbidity promptly ceases and the agglutinated micrococci fall to the bottom of the tube in a perceptible sediment. This is known as the "sedimentation test."

In control experiments with normal serum, turbidity, rather than a separation into a clear upper portion and sediment at the bottom of the tube, will be observed. An essential to success in these proceedings is certainty in the knowledge of the test culture. Controls with normal serum and dilution, and with dilution without serum, should be made, to exclude clumping or agglutination due to faulty cultures.

CHAPTER IX.

YELLOW FEVER.

Synonyms. Fiévre Jaune; Fiebre amarillo; Vomito negro.

Definition. Yellow fever is an acute, specific, infectious, febrile disease of a limited tropical distribution, noncontagious in character but occurring in epidemics and endemics. It is very fatal, but when recovered from produces immunity against subsequent attacks for the affected individual, this immunity being very general and permanent. The disease is caused by a specific organism or principle as yet undiscovered, and is communicated by a certain variety of mosquito, *Stegomyia fasciata*, and, in all probability, only in this way. The disease is clinically characterized by fever, sthenic in type at first and later becoming asthenic. It is remittent throughout. Other fairly constant symptoms are yellow discoloration of the skin, vomiting of a dark material, severe aching pain, especially in the head, limbs and loins, the occurrence of albuminuria and profound depression.

The jaundice of yellow fever is hematogenous in character and the black vomited material consists of blood, mucus, and the gastric secretion.

The infectious principle is definitely known to be blood borne, the disease being capable of transference to healthy persons by the injection of blood from the yellow fever patient, and it is further believed to be an invisible or ultramicroscopic body, the blood serum retaining its infecting power after passage through the Pasteur-Chamberland filter.

Facts of Geography and History. Principally confined to the American continents and islands, yellow fever has an extreme latitude range extending from forty-six degrees North (Quebec) to thirty-five degrees South (Buenos Ayres), having occurred in both of these places; but, in fact, it is confined principally to

the extreme southern portion of the United States, Mexico, the Islands of the Caribbean Sea, Central America, Venezuela, the Guianas and Brazil; in a general way being confined to the tropic and subtropic countries bordering on the Gulf of Mexico and to adjacent countries.

In Africa yellow fever is known in the West Coast (Sierra Leone and Gambie), but as it usually occurs in epidemics only, it is believed to be imported from the American tropics. It frequently extends from the Mexican Gulf region both north and south, along the coast, or ascends the great rivers, the Mississippi, the Amazon and occasionally the Paraguay. Being generally transmitted in ships along commercial water paths, the disease frequently appears in New Orleans, Charleston, and, occasionally, as far north as St. Louis and Memphis on the Mississippi. On the main land, however, it progresses by rail routes, but it never appears unless the distributing mosquito (Stegomyia fasciata) is present to convey the yellow fever poison, through its bites, to nonimmune persons. A map, therefore, showing the distribution of Stegomyia fasciata would also indicate the limits to which yellow fever might extend, provided the other necessary conditions, a case of yellow fever and receptive (nonimmune) individuals, were present. It must be remembered, however, that mosquitos are portable, and that new localities are constantly becoming infested with Stegomyia mosquitos, as well as with other varieties, pathogenic and nonpathogenic. Such a map, therefore, would require constant revision.

Accepting the modern view, we must admit that the only relations which season, meteorologic conditions, rainfall, wind, and altitude, bear to the endemicity of yellow fever are indirect and are active only as they affect, favorably or otherwise, the breeding and distribution of Stegomyia fasciata. Whether yellow fever was originally an African or an American aboriginal disease is a question which can never be definitely answered, and one which it is profitless to pursue. In any case, the disease has been definitely identified with the American tropics for more than two hundred years.

Europe has been invaded repeatedly by epidemics of yellow fever of greater or less severity. In every case, however, the infection was readily traced to ship communications with tropical America, especially with the ports of Havana, Vera Cruz, and Rio Janeiro, Brazil, and the disease showed little disposition to spread, a fact readily understood in the light of our modern knowledge of its infectiousness. Notable among the epidemics in Europe is that of Cadiz, Spain, in 1800, of Barcelona in 1821 and of Lisbon, Portugal, in 1857, when 5000 deaths and 18,000 cases occurred in two months. This epidemic was imported from Brazil, although the Spanish outbreaks were generally due to communication with Havana or Vera Cruz. One epidemic occurred in Italy and the disease was also introduced into England (Southampton, 1851, Falmouth, 1865, and Swansea, (Wales), 1865) from French ports communicating with Havana, Cuba, Mexico and the United States.

We will not undertake to follow the history of yellow fever in the United States. It visited the cities of the South and middle South so often that it came to be looked upon as a necessary accompaniment of summer in Charleston and other southern cities, Charleston alone having been visited by more than thirty recorded epidemics in the Nineteenth Century. It was formerly considered necessary to remove from the city during the summer months to escape the danger of infection. In 1793, 1797, and 1798, Philadelphia had severe visitations of yellow fever. The more notable epidemics which swept over the Southern States were those of 1853, 1867, and 1878. In the first two, Florida, Alabama, Louisiana, Mississippi, Arkansas and Texas were chiefly visited. But in 1878, when 75,000 cases, and 15,000 deaths occurred, the disease prevailed in the Mississippi Valley as far North as St. Louis; Memphis, Tenn., being especially afflicted.

In 1905, about 3400 cases, with 451 deaths, occurred in New Orleans, while in Pensacola, Florida, 560 cases with 80 deaths appeared. Scattered cases, from these foci, also occurred in the neighboring Southern States, chiefly in the vicinity of these cities.

In 1906, the disease failed to reappear in these centres, as a result of the wholesale destruction of Stegomyia mosquitos, during the previous year.

By far the most illuminating facts connected with yellow fever have been gathered within the past six years. A record of achievements which stands alone for daring of purpose, brilliancy of execution, finality of result and influence upon humanity, as evidenced by the complete eradication of yellow fever from its stronghold of centuries (Havana) in a few short months, is that of the American Yellow Fever Commission.

The facts are now historic and while the record of the original fever researches include matter which would naturally appear under the heading of etiology, the investigations and findings of the American Commission should be narrated here. Nowhere are they more completely and succinctly summarized than in the report of the Surgeon-General, United States Army, for 1901 (General G. M. Sternberg, United States Army, retired), which is as follows:

"BOARD FOR THE STUDY OF THE ETIOLOGY AND PREVENTION OF YELLOW FEVER.

"In my last annual report I referred to the appointment of a Board for the purpose of pursuing scientific investigation with reference to the acute infectious diseases prevailing on the Island of Cuba. This Board, consisting of Major Walter Reed, Surgeon United States Army, and Contract Surgeons James Carroll, Artistides Argamonte, and Jesse W. Lazear, United States Army, arrived at their station, Columbia Barracks, Quemados, Cuba, on June 25, 1900, and at once proceeded under written instructions from this office, published in my last Annual Report, to the special study of questions relating to the causation and prevention of yellow fever.

"Fortunately for the purpose of this board an epidemic of yellow fever, which had begun in the adjacent town of Quemados, Cuba, during the latter part of the month of May was still prevailing, so that an opportunity was afforded for bacteriological

and pathological observations in this disease. In the course of the investigations which were assiduously carried out by the members of the Board during the months of July, August and September, the results obtained, especially as relates to the mode of propagation of yellow fever by the bite of the mosquito, were such as to warrant their publication. For this purpose permission was given to Major Walter Reed, president of the board, to present a preliminary report at the meeting of the American Public Health Association held in Indianapolis, Ind., Oct. 22 to 26, 1900.

"In its experimental work during these months two of the members of the board suffered from yellow fever as the result of having been bitten by infected mosquitos. Dr. Lazear was bitten September 13, 1900, became affected with yellow fever five days afterwards, and died September 25, 1900. Dr. Carroll was bitten August 27, 1900, and was removed to the yellow fever ward on September 1, 1900. He suffered from a severe attack of the disease, but fortunately recovered. The conclusions of the board in its preliminary report were, first, that the Bacillus icteroides (Sanarelli) stands in no causative relation to yellow fever, but when present should be considered as a secondary invader in this disease; second, that the mosquito serves as the intermediate host for the parasite of yellow fever.

"As these observations, if confirmed, were of the highest importance in the future prevention of yellow fever, not only among our troops stationed on the Island of Cuba, but in our Atlantic seaports, the board was directed to continue its observations especially along the same line of investigation.

"With the approval of the military governor of the Island, an experimental station was established and further observations undertaken by Major Reed and his associates. A small camp of nonimmune young men, mostly belonging to the hospital corps, was formed in an open field about a mile from Quemados, Cuba. After this camp had been occupied long enough to show that yellow fever in its stage of incubation was not present, five of the men permitted themselves to be bitten by infected mosquitos.

In from three to five days each of these men became the subject of a well-defined attack of the disease and was sent to the yellow fever hospital. In a second series of experiments, four non-immunes were injected with blood from yellow fever patients. Each of these was attacked and sent to the fever hospital, while four of the men who had suffered an attack from infection transmitted by mosquitos manifested no bad effect from a similar injection of yellow fever blood. The mosquito-conveyed infection had given immunity from the disease. A third series of experiments was carried out to determine whether yellow fever can be conveyed by clothing and bedding which have been contaminated by contact with yellow fever patients, and their discharges. A small unventilated hut was built, its interior well guarded against mosquitos by wire screens. Dr. R. P. Cooke and two hospital corps men, all of them nonimmunes, passed twenty consecutive nights in this hut, sleeping in contaminated sheets and blankets taken from the beds of yellow fever patients in the Los Animas Hospital, of Habana, Cuba. After this a fresh stock of soiled articles, including pajamas, undershirts, and nightshirts, in addition to bedding, was obtained from the fever hospital and two nonimmunes occupied the room for twenty-one nights. A third time this experiment was repeated by two nonimmunes for twenty nights; yellow fever was not developed in any of these experiments. Meanwhile another small hut was constructed, well ventilated and with a wire screen extending from floor to ceiling in the middle, dividing it into two compartments. Every article before admission into this room was carefully disinfected by steam. Fifteen infected mosquitos were set free in one compartment into which a nonimmune hospital corps man entered and was bitten. Four days afterwards he was removed to the yellow fever hospital. The other compartment was occupied for eighteen nights by two nonimmunes whose health remained perfect. The conclusions drawn from these experiments were:

"1. The mosquito—Culex fasciatus—serves as the intermediate host for the parasite of yellow fever.

"2. Yellow fever is transmitted to the nonimmune individual

by means of the bite of the mosquito that has previously fed on the blood of those sick with this disease.

"3. An interval of about twelve days or more after contamination appears to be necessary before the mosquito is capable of conveying infection.

"4. The bite of the mosquito at an earlier period after contamination does not appear to confer any immunity against a subsequent attack.

"5. Yellow fever can also be experimentally produced by the subcutaneous injection of blood taken from the general circulation during the first and second days of the disease.

"6. An attack of yellow fever, produced by the bite of the mosquito, confers immunity against the subsequent injection of the blood of an individual suffering from the nonexperimental form of this disease.

"7. The period of incubation in thirteen cases of experimental yellow fever has varied from forty-one hours to five days and seventeen hours.

"8. Yellow fever is not conveyed by fomites, and hence disinfection of articles of clothing, bedding, or merchandise, supposedly contaminated by contact with those sick with this disease, is unnecessary.

"9. A house may be said to be infected with yellow fever only when there are present within its walls contaminated mosquitos capable of conveying the parasite of this disease.

"10. The spread of yellow fever can be most effectually controlled by measures directed to the destruction of mosquitos and the protection of the sick against the bites of these insects.

"11. While the mode of propagation of yellow fever has now been definitely determined, the specific cause of this disease remains to be discovered.

"Subsequent to this, and in continuation of the same line of experimental work, Major Reed and his assistants succeeded in inducing attacks of yellow fever in four other persons by means of the bites of mosquitos that had previously bitten yellow fever patients, thus making a total of twelve cases produced by the

bites of mosquitos. These latter cases were of special importance as showing the length of time during which the mosquito may remain capable of conveying the disease. In three of the cases the intervening period between the contamination of the insect and the production of the disease was thirty-nine, fifty-one, and fifty-seven days, respectively, thus offering an explanation of the fact that the contagion of yellow fever may cling several months to a building that has been vacated by its occupants, or to the infected area of a town, even though the latter has been entirely depopulated.

"Upon the recommendation of Major Reed further work at the experimental sanitary station near Quemados was discontinued at the end of February, 1901, and the members of the board were ordered to return to their proper station in this city, in order to give special attention to the search for the yellow fever germ in the bodies of the infected mosquitos which had been killed and preserved at various dates after their contamination. This investigation is still being carried on in the laboratory of the Army Medical School. I am very glad to be able to report that recovery took place in all patients, the subjects of experimentation.

"The importance and far-reaching consequences of the observations made by Major Reed and his associates at Quemados, Cuba, can hardly be overestimated. For the first time in the history of this widely prevalent tropical disease we are in possession of knowledge with regard to the manner of its propagation which will enable us, I believe, not only to check its ravages, but to effectually stamp it out wherever it may appear in any of our garrisons or cities."

Promptly recognizing the value of the preliminary work of the American Commission, the Liverpool School of Tropical Medicine in 1900–1901 sent Drs. Dunham and Myers to Para to conduct similar studies. Dr. Myers unfortunately lost his life on this expedition from an experimentally produced case of yellow fever.

Parker, Beyer, and Pothier, for the United States Public Health and Marine Hospital Service, verified the essential facts at Vera

Cruz, Mexico, and the Pasteur Institute Commission of France, Marchoux, Salimbeni, and Simond, conducted particularly excellent researches at Rio, Brazil, principally confirmatory of the American Army Board findings. The latest work is that of the German Commission, Otto and Neumann, in Brazil, whose report is just published. The conclusions of these various groups of scientists are in accord as to the correctness of the American commission's conclusions in 1900, in all essential points.

During the American invasion of Cuba by the Fifth Army Corps in the Spanish-American war in 1898, there occurred an epidemic of yellow fever among the American troops which nearly demoralized one of the most efficient small armies the world has ever seen. Disease might well have routed this army in a manner which Spanish bullets could never have accomplished, had the campaign been delayed and had the decisive land and sea victories of Santiago not been won early in the year, thus permitting the withdrawal of the American forces from an endemic yellow fever region.

In view of the popular misapprehension of this epidemic, and the oft-heard fictions relating to the prevalence of yellow fever in the American Army of invasion of 1898, the following remarks of the Surgeon-General, United States Army, quoted from his Annual report for 1899, are introduced here.

"During the calendar year, 1898, there were reported among the regular troops 604 cases of yellow fever, of which 70, or 11.6 percent., were fatal—576, with 67 deaths, in Cuba, and 28, with 3 deaths, in the United States. Most of the cases occurred at Santiago—in July, 462, with 25 deaths, and in August, 120, with 40 deaths, making 582 cases in the army of invasion, the 65 deaths constituting 11.2 percent of the cases. Twenty-two cases, five of which were fatal, were scattered through the remaining months of the year.

"It is very certain that these figures fail to give an adequate idea of the prevalence of this fever in General Shafter's army. In July and August, 1898, medical officers on duty with regiments in that army had few or no facilities for keeping accurate records.

On this account some of the cases treated in regimental camps were never reported. Indeed, it may well be believed that with so much prostrating sickness among them many men suffering from mild attacks did not even report themselves as sick. And when we consider the great prevalence of well-pronounced malarial fevers, the likelihood of some of the yellow fever cases appearing on the records as malarial remittents can easily be appreciated. Major Havard, chief surgeon of the Fifth Army Corps, found 300 men sick out of a strength of 740 in the Seventh Infantry, when camped near Cuevitas, about the middle of August. Two hundred and fifty of these were reported as affected with malarial fever and diarrhea, and fifty with yellow fever. Again, some of the medical reports, which describe the existing conditions in general terms, characterize the yellow fever attacks as being of a mild type, with a mortality scarcely so large as that of the malarial fevers which were so common at the same time.

"It is probable that many of the so-called mild cases of yellow fever were in fact cases of malarial fever. Indeed, the alarming reports received as to the general prevalence of yellow fever among our troops shortly after the surrender of Santiago were not sustained by subsequent events. It is now evident that the fever which prevailed so extensively in the Fifth Army Corps as a result of exposure in the trenches and in camps located in an intensely malarial region was, in fact, a severe type of malarial fever, due to the æstivo-autumnal parasite.

"The transfer of this army to the United States was effected without the occurrence of a disastrous epidemic on any of the crowded transports and without the introduction of yellow fever into this country, at a period of the year when there were still two months of a possible yellow fever season before us."

Credit for the original ingenious theory of mosquito conveyance of yellow fever is undoubtedly due to Dr. Carlos Finlay, of Havana, who announced his belief that the disease was thus conveyed from person to person, in Havana in 1881. The American Commission was undoubtedly influenced in the direction of its investigations by this theory, as well as by the accomplished

results in the investigations of malarial disease which followed the theorizing and discoveries of Manson, Ross, and the Italians. Finlay's other literary contributions relating to the mosquito propagation of yellow fever are dated in 1891, 1894, 1895, and 1899.

The incriminated mosquito, by a classification subsequent to the Havana investigations in 1900, was removed from the Culex variety and is now known as Stegomyia fasciata, rather than Culex fasciatus.

Etiology and Prophylaxis. Additional facts concerning the etiology of yellow fever have been developed by the various commissions referred to and may be briefly summed up as follows:

Blood drawn from yellow fever patients loses its infecting power if subjected to a temperature of 55° C. for ten minutes.

The incubation period of yellow fever varies from one to seven days, and occasionally even longer, the average being about three days.

All efforts to discover in the blood, or to isolate from it, micro-organisms or hematozoal bodies bearing causal relations to yellow fever have failed. The same is true concerning the search for such germs or parasites within the bodies of infected mosquitos. Every refinement of microscopy known, including the use of the ultramicroscope of Siedentopf and Zsigmondy by the German Commission in Brazil, has been resorted to.

Lieutenant Carroll, United States Army (Medical Department), a member of the yellow fever commission in Cuba, a victim of the experimental disease, and one of the foremost workers and authorities in yellow fever research and experimentation, gives the following reasons for believing that bacteria may reasonably be excluded as causes of yellow fever. (Address before American Association for the Advancement of Science, New Orleans, January, 1906.) (Journal American Medical Association, March 17, 1906.)

1. No bacterial organism has been stained or cultivated by any of our known methods.

"2. The work of Marchoux, Salimbeni, and Simond has shown that the blood of the patient after its withdrawal loses its

power to infect within two days, if kept exposed to the air, and within five days if air is excluded."

3. The demonstrated noncontagiousness of yellow fever where Stegomyia fasciata is absent.

"4. We know no bacteria that live in the tissues of animals, as the yellow fever organism does in the mosquito, for months, as a harmless parasite. The logical conclusion, therefore, would seem to be that the parasite of yellow fever belongs to the animal kingdom because (1) it is absolutely necessary for its continued existence that it pass alternately through man and the mosquito and its parasitic existence in these hosts is obligatory;" "(2) The fact that a period of about two weeks or more must elapse before the contaminated mosquito is capable of infecting, points to a definite cycle of development in that insect;" "(3) The limitation of its developmental cycle to mosquitos of a single genus, and to a single vertebrate, conforms to a natural zoologic law, and does not agree with our present knowledge of the life-history of bacteria;" (4) Carroll points out that climate and temperature have identical effects upon Stegomyia fasciata (yellow fever conveying) and Anopheles (malaria carrying) mosquitos so far as the development of yellow fever and malaria parasites within them are concerned.

Elsewhere in this work (Chapter on Hygiene) we have discussed and described Stegomyia mosquitos, their breeding habits, eggs, and favorite haunts, and, therefore, it will only be necessary to add a few facts relating to this particular insect. Stegomyia fasciata is essentially a house mosquito and does most of its biting by day. It dislikes both darkness and bright sunlight and makes but short flights, rarely more than one hundred yards. After gorging herself with blood the mosquito does not bite again for several days, in the meantime digesting her meal. As stated in previous pages, Stegomyia fasciata is often transported in ships and railway cars for long distances; aboard vessels its eggs are deposited in port and hatched at sea during the ship's voyage.

Concerning the hereditary transmission of the yellow fever organism in the mosquito, from insect to egg, American workers

have met with failure in repeated attempts to show that the eggs of infected mosquitos hatch into infected insects capable of propagating yellow fever without acquiring the poison from human blood. Marchoux and Simond report a case of yellow fever so induced and if their observation be confirmed, another and a most important means of mosquito conveyance of the disease will have be to dealt with. This question should be definitely determined at an early date. The article by Rosenau (June, 1906, Journal of the American Medical Association), deals with this question.

As mosquitos cannot obtain blood from corpses (unless there be exposed cut surfaces, as in the postmortem room, or blood containing discharges), the dead from this disease can safely be handled and need not be feared. Infected mosquitos have been known to live for over five months and to communicate the disease two months after becoming infected. They may also hibernate through the winter, probably retaining their power to infect from one season to the next. If this be true, the occurrence of fresh cases of yellow fever in the spring, in cities where the disease has prevailed in the preceding autumn, is explained, and the possibility of houses or cities retaining their infection from season to season, even when cold weather prevails for a few months intervening, may be understood. The bearing of these matters upon prophylaxis and the eradication of the disease is clear. Formerly the prophylaxis of yellow fever, as taught, included the destruction of many things believed to be capable of harboring and conveying the contagious principle of the disease. Today the gospel of destruction applies only to the mosquito, its lurking places and breeding places. There can be no belief in the doctrine of fomite infection in yellow fever for those who have carefully followed the experiments of the American yellow fever commission at Quemados, Cuba, in 1900 and 1901. So thoroughly convinced of the mosquito origin of every case of yellow fever are the authorities of Rio de Janeiro, Brazil, from their observation of the work of the French and German Commissions, and also of a Brazilian commission, carried on in Rio, that they expended more than

$500,000 in nine months to exterminate mosquitos in this city alone. A sanitary corps of 2000 men, including eighty medical men, looked to the details of isolation and screening of yellow fever cases, the destruction of breeding places of mosquitos in and about houses and the killing of the mosquitos themselves, public education as to the true cause and proper preventive methods in yellow fever and the necessity for the use of mosquito netting both by the sick and by the well. The successful campaign of Colonel Gorgas in Havana, against mosquitos, whereby yellow fever was banished from that city after more than a hundred years of continuous prevalence, is an object lesson which should ever be kept in sight and mind by sanitarians. Unfortunately, it is rarely possible to have the conditions under which Colonel Gorgas worked in Havana; available funds, trained assistants, absolute military control of the situation, and the support of the constituted authorities, headed by the military governor (General Leonard Wood, himself an experienced physician and sanitarian).

Given similar conditions in New Orleans the lamentable epidemic of 1905 would have been impossible. As indicating the proper prophylaxis of yellow fever and including all the essential details of prevention, applicable alike to a military post or any community where there is authority to carry out its provisions, the general order of the military governor of Cuba in 1901 (General Wood) is reproduced.

Circular.

No. 5. Headquarters Department of Cuba,
Habana, April 27, 1901.

Upon the recommendation of the chief surgeon of the department, the following instructions are published and will be strictly enforced at all military posts in this department:

The recent experiments made in Habana by the Medical Department of the Army having proved that yellow fever, like malarial fever, is conveyed chiefly, and probably exclusively, by the bite of infected mosquitos, important changes in the measures used for the prevention and treatment of this disease have become necessary.

1. In order to prevent the breeding of mosquitos and protect officers and men against their bites, the provisions of General Orders, No. 6, Department of Cuba, December 21, 1900, shall be carefully carried out, especially during the summer and fall. (Relates to screens, ditching, use of kerosene, etc.—T.W.J.)

2. So far as yellow fever is concerned, infection of a room or building simply means that it contains infected mosquitos; that is, mosquitos which have fed on yellow fever patients. Disinfection, therefore, means the employment of measures aimed at the destruction of these mosquitos. The most effective of these measures is fumigation, either with sulphur, formaldehyde, or insect powder. The fumes of sulphur are the quickest and most effective insecticide, but are otherwise objectionable. Formaldehyde gas is quite effective if the infected rooms are kept closed and sealed for two or three hours. The smoke of insect powder has also been proved very useful; it readily stupefies mosquitos, which drop to the floor and can then be easily destroyed.

The washing of walls, floors, ceilings, and furniture with disinfectants is unnecessary.

3. As it has been demonstrated that yellow fever cannot be conveyed by fomites, such as bedding, clothing, effects, and baggage, they need not be subjected to any special disinfection. Care should be taken, however, not to remove them from the infected rooms until after formaldehyde fumigation, so that they may not harbor infected mosquitos.

Medical officers taking care of yellow fever patients need not be isolated; they can attend to other patients and associate with nonimmunes with perfect safety to the garrison. Nurses and attendants taking care of yellow fever patients shall remain isolated, so as to avoid any possible danger of their conveying mosquitos from patient to nonimmunes.

4. The infection of mosquitos is most likely to occur during the first two or three days of the disease. Ambulant cases—that is, patients not ill enough to take their beds and remaining unsuspected and unprotected—are probably those most responsible for the spread of the disease. It is, therefore, essential that all

fever cases should be at once isolated and so protected that no mosquitos can possibly get access to them until the nature of the fever is positively determined.

Each post shall have a "reception ward" for the admission of all fever cases, and an "isolation ward" for the treatment of cases which prove to be yellow fever. Each ward shall be made mosquito proof by wire netting over doors and windows, a ceiling of wire netting at a height of seven feet above the floor, and mosquito bars over the beds. There should be no place in it where mosquitos can seek refuge, not readily accessible to the nurse. Both wards can be in the same building, provided they are separated by a mosquito tight partition.

5. All persons coming from an infected locality to a post shall be kept under careful observation until the completion of five days from the time of possible infection, either in a special detention camp or in their own quarters; in either case their temperature should be taken twice a day during this period of observation so that those who develop yellow fever may be placed under treatment at the very inception of the disease.

6. Malarial fever, like yellow fever, is communicated by mosquito bites and therefore is just as much of an infectious disease and requires the same measures of protection against mosquitos. On the assumption that mosquitos remain in the vicinity of their breeding places, or never travel far, the prevalence of malarial fever at a post would indicate want of proper care and diligence on the part of the surgeon and commanding officer in complying with General Orders, No. 6, Department of Cuba, 1900.

7. Surgeons are again reminded of the absolute necessity in all fever cases to keep, from the very beginning, a complete chart of pulse and temperature, since such a chart is their best guide to a correct diagnosis and the proper treatment.

By command of Major General Wood.

H. L. Scott, Adjutant General.

Pathology. In a disease known to be blood borne, as is yellow fever, we naturally seek, first of all, for pathologic changes in this fluid. As a matter of fact, however, the changes to be noted are

principally such as occur in infectious diseases generally, no characteristic germs or parasite having been discovered therein. Numerous false alarms concerning the discovery of specific micro-organisms peculiar to yellow fever, which have been announced from time to time, need scarcely be related. Authoritative medical works, if recently revised, no longer recognize any of the various causative organisms, announced from time to time, as authentic.

In former days when yellow fever was treated by venesection, the red color of the serum and incomplete coagulation after the shed blood was allowed to stand, was noted by clinicians. Modern observers now find that there is an abnormal amount of free hemoglobin in the plasma, involving, of course, a loss of hemoglobin from the red cells. The individual cells, however, often seem to contain more than a normal amount of hemoglobin. The red cells do not show great variation in numbers but there may be increase or diminution of the white corpuscles, leucocytosis being generally considered a favorable omen. During convalescence the leucocytes are also increased, as a rule, and the red cells show a reduction in numbers and in hemoglobin value. The frequency of hemorrhage in yellow fever is ascribed by some to capillary fatty degeneration.

In the urine, which is generally albuminous in yellow fever, we find evidence of acute diffuse nephritis, granular and other casts being present. The *kidney*, upon postmortem examination, is swollen, the cortex may be hemorrhagic, the glomeruli are hyperemic, and fatty degeneration of the renal epithelium is present in advanced cases. The kidneys are generally of a brownish yellow color, decidedly lighter than normal.

The characteristic yellow color of the skin and conjunctivæ, from which the disease takes its name, is of varying degrees of intensity, ranging from a faint yellow tinge to a golden or saffron yellow. The more intense color is often observed after the disease has existed for some days. The presence of urobilin, bilirubin and biliverdin has been detected in the urine and blood serum, by the spectroscope and by chemical analysis. Whether

the discoloration is due to these biliary pigments or to the presence of free hemoglobin in the blood, or to both, is not entirely clear as yet. After death, ecchymotic spots, due to passive hemorrhages, are also observed at times upon the face, trunk and extremities. All of the viscera exhibit evidences of acute fatty degeneration, and in the *liver* this degeneration is especially apparent. In addition, this organ is firm, dense, and friable, of a yellow color throughout, varying from pale shades to very dark yellow. There is usually enlargement of the liver, especially of the right lobe, and it may be adherent to relating structures. If death has occurred early it may be found engorged with blood, but usually is not so. The color is the most characteristic feature of the macroscopic appearance. When the gall bladder contains bile it is usually extremely dark, thick and sticky. Definite areas of necrosis are plainly evident throughout the liver.

The *pancreas* is yellowish and enlarged and there are evidences of acute fatty degeneration.

Generally speaking, the *spleen* in yellow fever is but slightly enlarged, and it often presents no variations from the normal. The pigmentation of malarial fever and the evidences of blood destruction generally, are absent, unless there has been a preceding malarial infection.

The *adrenals* also show evidences of acute fatty degeneration.

The *heart* shows the changes of acute fatty degeneration, being soft and flabby. Upon microscopic examination granular matter and oil globules are observed to be deposited in and between the muscular fibres. The pericardium is congested and the pericardial fluid may be deep yellow in color.

The *lungs* show no changes in yellow fever.

The meninges of the *brain and cord* and the cerebro-spinal fluid are tinged with yellow, and upon section the brain may even be golden yellow. The blood vessels are more or less engorged and there may be minute hemorrhages throughout the brain substance. No other characteristic lesions are found, except that the acute fatty degeneration referred to extends to the small blood vessels of both brain and meninges.

The urinary *bladder* presents no pathologic evidences other than those of congestion.

The *stomach* and *small intestine* present important pathologic changes, but the *large intestine*, except for congestion of the mucosa, is not altered. In the stomach, which is dilated and usually contains a variable amount of black fluid, undigested foods, and medicine, we observe that the mucous membrane is not only congested but actually eroded in places, the abrasions usually occurring in furrows, and at either or both cardiac and pyloric ends of the organ. Desquamation and hemorrhage, evidenced by the presence in the black stomach contents of blood and cellular elements from the mucosa, are apparent, and extend to the upper intestine, especially the duodenum. In the small intestine intussusception is often observed. The intestinal tube is dark in color and distended with gas. Blood may be present within it. While the stomach contents and the contents of the small intestine are usually strongly acid, they may be alkaline in reaction, due to the presence of ammonia derived from the decomposition of urea which is eliminated by the gastro-intestinal mucosa. The degree of congestion of the gastric and intestinal mucous membrane varies in different cases, but is usually well marked. Punctate ecchymoses of the gastric and intestinal mucosa, especially in the duodenum, may be considered as characteristic in yellow fever.

Symptoms and Treatment. The various gradations in severity and the predominance of certain symptoms and groups of symptoms have given rise to the clinical separation of yellow fever into numerous varieties. These include the so-called abortive, larval, mild, severe and fulminant varieties, and the renal, hepatic, hemorrhagic, and cardiac forms of the disease.

In the hepatic form (acholic) the suppression of the normal bile flow into the intestine and the wide dissemination of biliary pigments throughout the fluids and tissues of the body, together with hepatic swelling and tenderness are especially apparent.

In the renal form the suppression of urine, either complete

or incomplete, and the resultant evidences of uremia, delirium, coma, and convulsions, are most prominent.

In the cardiac variety of the disease arhythmia, rapidity of the pulse, cardiac weakness or actual cardiac paralysis may appear; while the hemorrhagic variety is marked by black vomit, petechial hemorrhages and hemorrhages from the intestinal mucosa. In view of the frequent overlapping of these clinical types, nearly every case combining one or more of the symptoms of several types, and in view of the probability or practical certainty that these localizations of symptoms simply indicate a local poisoning from a systemic toxin, doubtless circulating in the blood, we will consider the symptoms of yellow fever without particular regard to their localization of expression.

Although yellow fever is sudden of onset as a rule, cases do occur in which vague prodromes appear from twenty-four to seventy-two hours before the fever sets in, that is, immediately following the infecting bite of the mosquito. This prodromal period is also known as the period of "intrinsic incubation." When they occur, these prodromes consist of loss of appetite, headache, weariness, and a sense of impending sickness. Usually a sharp, severe chill, or a succession of slight ones, is promptly followed by a rise of temperature and acceleration of the pulse; the temperature possibly rising to 104° F. and the pulse to a rate of 120 beats per minute. Headache and backache are present from the outset, and without delay the countenance and conjunctivæ become suffused with blood, photophobia and an expression of mingled apathy and anxiety appearing. There is as yet no icteric discoloration and there may be no gastric disturbance, either nausea or vomiting, during these early hours of yellow fever. In a short time, if not from the first, the tongue takes on a white or gray coating along its middle, the borders remaining red or becoming abnormally so, the tongue generally being narrow and pointed in contrast to the broad, flabby, teeth-indented tongue of malarial fever. The aching, which is a marked symptom during this stage of the disease, is very severe in character and has been compared to the aching which occurs in the early stages

of smallpox. It also resembles the aching pains of dengue, and is sometimes described as bone-breaking in character. The loins and lumbar regions and the lower extremities are principally affected in this manner, and the pain is supposed to be due to meningeal hyperemia, both cranial and spinal.

The peculiar facies of this stage of yellow fever, the so-called "masque amaril," consists of a diffuse redness, sometimes approaching that of one of the acute exanthematous diseases, bright, glistening eyes with injected conjunctivæ and dilated pupils. Within a short time tenderness over the region of the stomach appears and pain is elicited by pressure over the duodenum or the pyloric end of the stomach. Nausea is complained of and bilious vomiting may occur. Hemorrhagic vomiting is not always present, and when it does occur usually succeeds this stage. It is, of course, a symptom of grave import. The symptoms just described belong chiefly to the first stage of the disease, or the period of onset and invasion; also called the inflammatory period. Albumin usually appears in the urine at this stage but its appearance may be delayed. Although there is usually a subsidence of the congestive symptoms at the end of forty-eight or seventy-two hours, the so-called period of calm or remission is not by any means constant. The temperature may approach normal upon the fourth day but the subsidence of fever is gradual and not usually by crisis.

The pulse rate of yellow fever is most distinctive. During the high temperature of the first two or three days, it reaches 110 or more, and then loses correspondence with the temperature and respirations, often declining to fifty or even forty beats per minute. Its volume and hard character are also lost.

The patient is restless and unable to sleep during the first period of yellow fever, but delirium is not the rule, and restlessness is succeeded in the second stage by an apathetic mental attitude, or even by a comatose state. At the end of three days icterus, either pronounced or moderate, sets in, the yellow color appearing in the whites of the eyes if nowhere else. The skin may gradually become orange yellow in color, and this color persists both after death and during convalescence.

The second period is marked either by a remission or by increased intensity of the symptoms. Rarely a calm of forty-eight hours, during which the temperature remains at about 100° F., is followed by immediate convalescence. The period of calm, however, is quite as likely to be absent, and in this case, the intensification of symptoms following the period of onset is progressive,

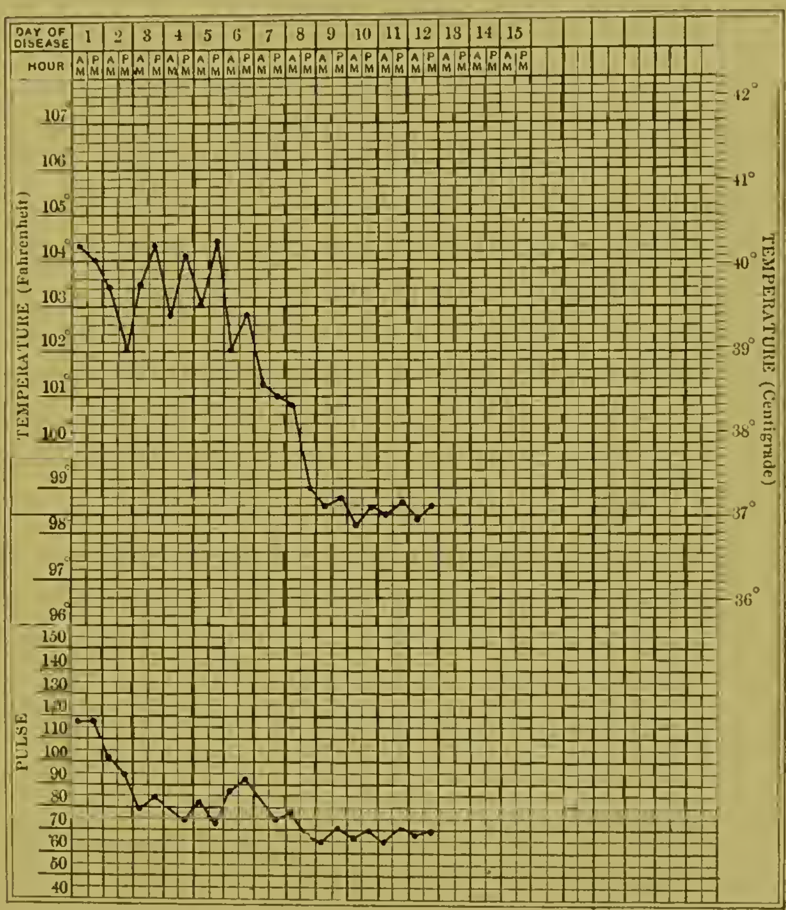


Fig. 67.—Clinical chart of yellow fever showing the pulse typically slow in comparison to the height of the temperature. (From Wilcox.)

the gastric symptoms, hemorrhages, yellow discoloration, kidney involvement, and the prostration of heart and circulation proceeding uninterruptedly. The urine is diminished in quantity, acid in reaction, and rich in albumin. The albumin may equal seventy-five percent of the total urine, by volume. Anuria may

be complete. The pulse decreases in strength and rate and becomes easily compressible. The eruptive symptoms usually described in connection with yellow fever are probably only such as are observed in many other febrile diseases, especially those accompanied by disturbance of the digestive function, and consist of urticaria, herpes of the face, and erythema. Hemorrhages into the skin have also been mentioned as expressions of acute fatty degeneration of the capillaries.

The symptoms rarely persist in their greatest intensity longer than three days, a general and progressive moderation setting in after this time, unless the disease prove fatal.

The urine may now become more abundant, lighter in color, and freer from albumin. The tongue regains its normal appearance and the vomiting ceases. Natural sleep occurs, and the pulse recovers its normal volume and rate. The temperature declines to normal or subnormal and remains there.

We have described an average case of yellow fever but it must be remembered that clinically the disease may vary considerably. For example, we meet with cases which are distinctly abortive, and others which are prolonged, lysis being so gradual that typhoid fever is simulated, the disease lasting for more than two weeks. The type of fever is sometimes continuous and it may also be intermittent in two or three paroxysms. Cases may also be fulminant, hyperpyrexia preceding death in the period of onset, or choleriform, diarrhea, algidity, aphonia, and anuria being present.

Relapses are rare in yellow fever but are not unknown. Complications, due to secondary infections with bacteria, especially those found in the intestine or the pyogenic varieties, are common enough and often protract convalescence, especially if suppurative processes occur in any part of the body. There are no distinctive sequels to yellow fever. Naturally, the subjects of a disease so debilitating as yellow fever are for a time particularly susceptible to other infections, the only immunity conferred being that against yellow fever itself.

Constipation is frequently present in yellow fever, and is an unfavorable condition.

According to the state and clinical variety of yellow fever the skin will be hot and dry, or moist and algid. Sweating is at times very profuse, especially during the preagonal stage. The skin or perspiration is said to give off a peculiar, offensive odor, but this observation is not usually accepted as correct. Although delirium is not a marked symptom of yellow fever and is usually absent, it sometimes occurs, especially during the stage of hyperpyrexia and it may even be of a violent character, requiring bodily restraint.

The *prognosis* is grave, in individual cases, according to the severity of gastro-intestinal symptoms, the degree of renal involvement, and the temperature range (106° F. being fatal in nearly all cases). In certain epidemics the mortality is high; in others it is low. Making due allowance for a variation in the death rates of different epidemics a mortality of twenty-five percent is not far from the average rate. Some years ago Sternberg critically studied 269 cases of yellow fever and found that in 44 cases in which the temperature remained below 103° F. there were no deaths.

In 22 cases in which the temperature exceeded 106° F. there were no recoveries. In 36 cases in which the maximum temperature attained was between 105° and 106° F. there were 22 deaths. In 80 cases in which the maximum temperatures were between 104° and 105° F. there were but 24 deaths; and in 87 cases, where the maximum temperature was between 103° and 104° F. only 6 deaths occurred. The mortality rate for the series of 269 cases was about twenty-seven percent.

A high percentage of albumin in urine is compatible with recovery if the amount of urine is abundant, or but slightly suppressed. Complete suppression for twelve hours is nearly always followed by death.

Certain facts concerning susceptibility to yellow fever have long been recognized and while all are not yet satisfactorily explained they are generally accepted as true. The first of these relates to race. Negroes are generally accredited with a definite, relative immunity to yellow fever. This immunity is by no means com-

plete but it is fairly well marked, and has been ascribed to a distaste on the part of the mosquito for the negro's skin, possibly on account of its offensive emanations or its thick dense character, or both. Yellow skinned persons are also supposed to be less susceptible than whites, and old residents (whites) of regions where yellow fever is endemic seem to be somewhat protected from infection, and when infection is acquired suffer less serious attacks than recent comers in the district. Whether or not this protection is acquired by unrecognized attacks in early life is doubtful, children as a rule escaping the disease. The most susceptible age seems to be that between sixteen years and thirty years. Sex is probably negative as a predisposing factor.

Treatment. While the treatment of yellow fever is purely symptomatic, there are definite indications to combat certain failing functions and vicious abnormal conditions. The renal and cardiac functions, in particular, and the temperature, demand special attention owing to their direct bearing upon life itself. Generally, we are called upon to combat vomiting, constipation, jaundice, urinary suppression, hyperpyrexia and cardiac failure. We will, therefore, consider these indications separately. Bilious vomiting may be treated initially by washing out the stomach, either by a syphon tube, or by copious draughts of hot water, alkaline in reaction. This is especially important if the stomach contains food, but should not be repeated after the organ is well emptied and flushed. Formerly an initial emetic was administered.

In a personal communication an experienced Army Surgeon, whose opinion I regard highly, rejects the proposition to use the stomach tube entirely and urges that the use of emetics be restricted to cases where there is clear evidence of overloaded stomachs. He also enjoins starvation, as a rule, during the first twenty-four hours. His rule is absolute quiet of the entire body and particularly of the stomach; the patient not being permitted to sit up or to help himself in any way. He regards this as the most important measure in the treatment of yellow fever. Not a few experienced men limit their medicine giving to a single laxative dose, administered during the first twenty-four hours.

Constipation, a most unfavorable state of the alimentary canal, should be vigorously treated at the outset. It is quite as important to have the digestive tube unloaded and free from fermenting undigested food and fecal matter as it is to have the stomach clean and empty. Antiseptics can be advantageously combined with cathartic drugs with an aim to secure conditions unfavorable to bacterial multiplication; complete sterilization of the intestine, of course, being unattainable. These efforts should not be delayed. Calomel combines with its certain purgative action the advantage of being an antiseptic, and should be given in sufficient dosage to get prompt results, ten grains, at least, being administered to adults. Castor oil is of value because of its mildness and certainty of action but is objectionable on account of its taste. Magnesium sulphate or the effervescing salts are useful and these likewise may be given in efficient doses. An ounce of magnesium sulphate, either in one or two doses, is an appropriate amount for an adult. After the first day or so, daily movements of the bowel may be secured by enemas of warm solutions of magnesium sulphate with glycerine, thrown well up into the colon. Salol or carbonate of guaiacol will serve to antisepticize the intestine and these may be given in a few full doses in the early stages of the disease. As a rule, however, drugs which may give rise to kidney irritation should be avoided.

The treatment suggested and made popular by Sternberg consists of administering liberal amounts (one and one-half ounces every hour) of an alkaline, antiseptic solution, made by dissolving two and one-half drams of bicarbonate of sodium and one-third of a grain of bichloride of mercury in a quart of water. The objects sought in this treatment are rational in every sense, the treatment being directed at the kidneys, increasing their secretion, and the intestine and stomach which are antisepticized and alkalinized. Sternberg secured a death rate of 7.3 percent in a series of 300 white persons so treated. The icterus of yellow fever is principally combated by diet, an exclusive milk diet being adopted when it is possible to administer it.

Suppression of urine is perhaps the most dangerous symp-

tom of yellow fever and should be combated with milk diet, hot baths, either local or general, lumbar cupping, hot wet packs about the loins, and when occasion demands it, by the hypodermatic injection of pilocarpine hydrochlorate in doses from one-sixth to one-fourth of a grain. Pilocarpine may also be given by the mouth and should always be used with caution on account of its depressant heart action. It acts by relieving the kidneys of their work and placing it upon the skin, rather than by increasing the output of urine.

Hyperpyrexia, as has been shown, is excessively dangerous, and fever, therefore, should be controlled. External measures rather than internal medicines are to be chosen, and we have a variety of ways in which to apply cold. These include the use of ice cooled water, sponging, the ice bag, ice cold enemata, and the cold pack. The coal-tar derivative antipyretic drugs should rarely be used, if at all, on account of their well-known action upon the blood, destroying the red cells and converting hemoglobin to methemoglobin, and on account of the cardiac depression which many of them produce. Without doubt they do add to the patient's comfort when used, however. A mixture of equal parts of water, alcohol and vinegar is useful for sponging, and it may be used at any desired temperature and as frequently as necessary, according to the height of the fever. The use of hot drinks, teas made of various domestic leaves and herbs, is much affected by certain practitioners of the Southern States, and probably does no harm, and in so far as it promotes skin and kidney activity may do good. Diluents are generally preferable to diuretics in yellow fever, and ice is usually refreshing to the patient, and if given judiciously, may be sedative to the stomach. Ice pellets are usually permissible, but large draughts of ice water should be withheld. The circulation requires supportant remedies from the earliest period of the second stage and alcoholic stimulants are generally preferred, providing the stomach will retain them, on account of their diffusibility and prompt action. Champagne or brandy, or whiskey, are the most useful and the dosage should be small and frequently repeated. It is better to give

teaspoonful doses of brandy, or even of champagne, than to produce vomiting by larger amounts. If productive of vomiting, alcohol should be discontinued, and digitalin or nitroglycerine, or both, should be used hypodermatically. The symptom of vomiting may be intractable or difficult to control. Mustard plasters over the stomach and small doses of cocaine, bismuth or creosote may be required. By rectal injection, chloral hydrate, in fifteen grain doses, sometimes succeeds in allaying vomiting when all ingested medicines are rejected, and at the same time it may produce sleep.

The matter of *diet* is of great importance, and in yellow fever it is safer to administer only liquid foods, and generally during the first stage of the disease even these should be withheld. Alkaline carbonated waters may be given, however, and later these may be combined with milk (as, for example, Vichy and milk), and a liquid diet of barley water, chicken broth, and plain or peptonized milk may be established. This should be maintained, in spite of the patient's desires, until the gastric mucosa has time to recover from its intense congestion and becomes able to take up the work of digestion. Without doubt many cases of yellow fever die from injudicious feeding.

The nursing of yellow fever is of the utmost importance, and should be entrusted only to experienced persons, capable of carrying out to the letter the physician's directions and orders. Moreover, the nurse should be one without fear of the disease, preferably an immune person, and one capable of conveying confidence and of dispelling some of the dread so apt to seize patients ill with yellow fever; one capable of recognizing emergencies and of initiating intelligent action at such times.

To revert to the all important matter of Prophylaxis: we must remember that herein lies our greatest duty in the treatment of yellow fever, and that the most important feature of the treatment is the complete and perfect isolation of each patient from mosquitos. The early recognition and isolation of mild cases is absolutely necessary, as a mild case is perfectly capable of giving rise to the disease in a severe and fatal form in the next individual

24

inoculated. Small meshed wire mosquito netting, covering a portable and folding framework of generous size, which may be placed over and around the patient's bed, is the most effective device to prevent mosquitos reaching the patient. In addition to this we must destroy all the mosquitos which have had access to the patient preceding his illness, in so far as it is possible. The fact that these mosquitos do not, of themselves, travel far abroad, makes it probable that they are still within the house. Their breeding places, of course, should be destroyed. Even though the premises seem to be free from mosquitos, it may safely be assumed that they are present, or that the yellow fever patient has visited some place infested by them within a few days. It, therefore, becomes an important duty for the sanitary corps to investigate the movements of a patient stricken with yellow fever for the previous few days, in order to destroy the mosquitos which communicated the disease to him, and so to prevent further infection from them.

The experiments and conclusions of the French (Pasteur Institute) Commission in Brazil in the matter of immunizing and therapeutic sera from convalescent yellow fever patients do not as yet put us in possession of a tried and proven serum treatment for yellow fever, but they hold out to us hopes that we may eventually be able to prevent, treat and cure the disease by immunizing or antitoxic serum administration.

Diagnosis. The diagnosis of yellow fever, as well as the treatment, is purely symptomatic. We are, unfortunately, without the aids of serum diagnosis and microscopic blood examinations in the direct diagnosis of yellow fever, but both methods assist us in the differential diagnosis, by determining the exclusion of other suspected diseases.

The diseases most apt to be confounded with yellow fever, on account of their clinical similarity, and also on account of their geographic distribution and seasonal prevalence, are dengue and the malarial fevers. These three affections are endemic in the same latitudes and under the same conditions, and at least two of them are propagated in the same manner; by the intermediation

of mosquitos. In the early days of an epidemic of yellow fever the disease is frequently mistaken for dengue until postmortem diagnosis declares the existence of the graver disease. Moreover, the two diseases frequently exist epidemically at the same time. Under such circumstances diagnostic mistakes are easily understood and are not always inexcusable. It is, however, of the highest importance that the first cases of epidemic yellow fever be recognized, and it is, therefore, safer to suspect yellow fever than dengue, when doubt exists.

In a personal communication from an experienced medical officer of the Army who passed through epidemics of both yellow fever and dengue in Texas, he states that the clinical resemblance between the two diseases is so close that the first cases of an epidemic of yellow fever are invariably called dengue. He also states that jaundice, slow pulse, and albuminuria were present in some of his cases of dengue and that the rash was not always observed. The accompanying differential table may be useful, however, in discriminating between these diseases, and is compiled from the usual clinical manifestations of yellow fever, dengue, and malarial fever. The exceptional variations in dengue should be borne in mind, however, in its use.

	YELLOW FEVER.	DENGUE.	MALARIAL FEVERS.
Temperature.	Fever of one paroxysm, as a rule. High temperature for 3 days.	Fever of two paroxysms and a remission, as a rule. Fever high in first period; low in second.	Fever of several paroxysms with remissions or intermissions. Moderate temperature, as a rule.
Duration of Fever.	3 to 7 days.	5 to 8 days.	Variable duration. May last weeks.
Incubation.	Human incubation, 1 to 6 days. Mosquito incubation, about 12 days.	Short incubation 1 to 5 days; average less than 3 days.	Human incubation, 1 to several days. Mosquito incubation, about 10 days.
Vomiting.	Very common symptom —both bilious and hemorrhagic (black vomit).	Not common. Bilious vomiting in some cases.	May or may not be present. Bilious in character.

	Yellow Fever.	Dengue.	Malarial Fevers.
Pulse.	At first, rapid and bounding; later, abnormally slow and soft. Does not correspond with temperature.	Corresponds with febrile temperature.	Corresponds with febrile temperature.
Jaundice.	Characteristic and constant.	Rare.	Subicteric jaundice rather common.
Eruptions.	Rare and not characteristic.	Common and distinctive.	Rare and not characteristic.
Urine.	Scanty; often completely suppressed, and albuminous from early stages.	Quantity ample. Rarely albuminous.	Not usually albuminous nor suppressed.
Mentality.	Apathy common. Consciousness preserved as a rule.	Preserved.	Delirium not uncommon.
Hemorrhagic Symptoms.	Frequent and often fatal. (Gastric and intestinal chiefly.)	Of rare occurrence and of slight consequence.	Rare except in pernicious cases and in malarial hemoglobinuria.
Fatality.	Average mortality 25 per-cent.	Non-fatal.	Rarely fatal if treated properly.
Convalescence.	Rapid and without sequels.	Rather prompt but with arthralgic and myalgic sequels.	Slow, succeeded by anemia, and is apt to recur.
Immunity.	One attack confers subsequent immunity.	Doubtful immunity.	No immunity.
Response to Treatment.	Abortive or curative treatment negative.	Symptomatic treatment alleviates.	Satisfactory, specific (quinine) treatment cures.
Blood Condition.	Incomplete coagulation and free hemoglobin in serum. Red cells not greatly altered. White corpuscles either increased or decreased.	Leucocytosis common. Decreased leucocytes claimed by some observers.	Malaria parasites and pigment present. Leucopenia with a relative increase of large mononuclear leucocytes, the rule.

In the article upon yellow fever in Gould and Pyle's Cyclopedia of Medicine and Surgery (Blakiston, Philadelphia), the following statement, which seems to me to be very pertinent, is made: "The symptoms that have hitherto been relied upon to differentiate yellow fever and dengue are the occurrence in

the former of albuminuria, the characteristic facies (inclusive of jaundice), the divergent pulse and temperature, and excessive irritability of the stomach, and passive hemorrhages. The absence of such symptoms in the main, the presence of an eruption, and want of mortality in connection with the ordinary febrile phenomena are considered as characteristic of dengue. The diagnostic significance of the foregoing symptoms requires modification, that is to say a careful examination of the urine in cases of undoubted dengue may demonstrate a mild and evanescent albuminuria. A certain proportion of these cases may have slight jaundice, severe nausea, vomiting, and a disposition to passive hemorrhages from mucous membranes. Aside from the increased mortality of yellow fever and the characteristic postmortem findings, the differential diagnosis between these two diseases can be made by the symptom-complex of an acute nephritis in yellow fever and its absence in dengue. In the latter disease simple parenchymatous changes may occur in the kidneys, manifested by a slight and temporary albuminuria; while in the former, in a series of cases, many will afford incontestable evidence of a severe nephritis; viz.: Scanty urine, of high color and specific gravity, intense and persistent albuminuria, hematuria, casts, a decided tendency to suppression and the accompanying uremia. There is no authority who will claim that a serious kidney involvement belongs to the pathology of dengue; on the contrary it is universally conceded that the nephritic complications dominate the clinical picture in every severe case of yellow fever."

A normal or increased percentage of hemoglobin is the rule in yellow fever while in the malarial fevers the percentage is decidedly decreased.

Ehrlich's diazo reaction is not reported as occurring in yellow fever but it has often been observed in the urine of dengue and enteric fevers, in the latter disease being accorded diagnostic value by some writers.

The possibility of mistaking yellow fever for pernicious malarial fever is emphasized by the experience at the military post of Pinar del Rio, Cuba, in the spring of 1900. For more than

a year immediately preceding the outbreak of yellow fever I was stationed at this post and one of my duties (self-imposed at first) was the examination of the blood of all fever cases admitted to the hospital. Systematic and microscopic diagnosis was thus assured and during my service no case of yellow fever was admitted to the hospital nor was the disease at any time present, so far as known, in the town, although there was daily communication with Havana where yellow fever prevailed. Upon a few occasions cases were detained in isolated tents, under suspicion, until microscopic or therapeutic diagnosis could be established. The only two febrile diseases which prevailed during the year were malarial and typhoid fevers, the latter disease occurring epidemically for a short time. Elsewhere I have referred to the 1900 cases of malarial fever (with but four deaths) observed at Pinar del Rio during this period.

I was ordered to the United States on account of sickness in April, 1900. After my departure from this station the systematic blood examination of all fever cases was abandoned (as I have since been personally informed by one of the surgeons who remained on duty at Pinar del Rio barracks), partly from a false sense of security against yellow fever and partly from a lack of familiarity with microscopic work, or a lack of inclination towards it, on the part of the surgeons who remained on duty there.

The following is the official report of the outbreak of yellow fever at Pinar del Rio (Surgeon-General's Report for 1900, page 171), thirty-two cases with twelve deaths occurring. Without doubt this epidemic, or at least the failure to recognize the disease, was due to the discontinuance of systematic blood searches in all cases of fever admitted to the hospital.

"At Pinar del Rio Barracks a sergeant of the First Infantry was taken sick May 10 and died on the sixteenth with what was recorded as pernicious malarial fever. Another case was reported June 14 and four others were taken on sick report during the remainder of the month. Only one of these five cases recovered. Twenty-seven men, four of whom were civilians, became affected in July; eight of these died. The epidemic was suppressed by

the removal of the troops into camp about three miles from the barracks. Only two cases occurred in the command after the infected barracks were abandoned. This move should have been made much earlier."

The reports from the Panama Canal Zone indicate that nearly all of the cases of yellow fever there have occurred in malarial subjects, their blood showing the hemamebas. This is probably true of other regions where both diseases abound, and in consequence we must consider the absence of malaria parasites in suspected fever cases as important in excluding malaria but their presence inconclusive as to the presence or absence of yellow fever.

Other diseases which might, conceivably, be mistaken for yellow fever are Acute Yellow Atrophy (Icterus Gravis), Acute Phosphorus Poisoning, Acute Febrile Icterus (Weil's Disease), and Acute Catarrhal Jaundice.

The first of these diseases is more common in pregnant women and is not a tropical disease. Its causation, symptomatology and pathology are somewhat obscure. In phosphorus poisoning the history will suffice to clear up a doubt. Acute febrile jaundice has already been discussed and Acute Catarrhal Jaundice should not long be mistaken.

The divergence in the pulse rate and the temperature, according to what is known as Faget's law, is a valuable diagnostic occurrence in yellow fever and is depended upon with considerable assurance by practitioners in the Southern United States. We have already described this divergence which generally becomes apparent during the first two days of yellow fever.

In considering *epidemics* of dengue or yellow fever from the diagnostic view-point it will be helpful to remember that while both occur in the tropics, yellow fever has a much more limited distribution than dengue. Dengue usually affects a great majority of the inhabitants and the epidemic is spent within a few months, while yellow fever affects a far smaller percentage of the population and the epidemic may be indefinite in duration, provided frost does not cause the destruction or hibernation of Stegomyia

mosquitos. Dengue attacks all persons indiscriminately, while yellow fever singles out the nonresidents, especially Europeans and Americans.

Much has been written of late concerning the dangers to Asia and the Pacific Islands of the importation thereto of yellow fever from its home in the West Indies and Central America, by way of the new Panama Canal in process of construction. While the canal will not be completed for at least a decade, and the old injunction about not crossing a bridge before one reaches it appears to fit the case, we can, it seems to me, view this somewhat remote danger to the Orient hopefully. If medical science keeps up the pace at which it has progressed during the past five years, particularly with regard to knowledge of yellow fever, its prevention and causation, we will be able not only to prevent its exportation to the Far East but to witness its complete disappearance from the American continents and islands. A more immediate danger lies in the possibility of a severe visitation of yellow fever to the Canal Zone itself and a repetition of the horrors of the Canal building days of the French. If this danger is successfully met and averted, as it seems more than likely to be, under the able sanitary generalship of Colonel Gorgas, we may take hope for the future. In the meantime, without the Panama Canal, commercial intercourse between the western shores of Central and South America and the Orient (Honolulu, Japan, the Philippines and China), is sufficiently increased to make necessary an extremely rigid quarantine supervision of ships and persons. With our modern knowledge, the formidable quarantine requirements of disinfection of person, clothing, and cargo are unnecessary, so far as yellow fever is concerned. The exclusion of mosquitos from ships and the detention of passengers, preferably after boarding the vessel, for four days, in order that any developing cases may be detected, are all-sufficient. Even without further additions to our knowledge of yellow fever we have, in the proven guilt of Stegmoyia Fasciata mosquitos, the clue and key to sanitary salvation of our Pacific tropical possessions.

PART II.

ANIMAL PARASITIC DISEASES.

CHAPTER I.

ANKYLOSTOMIASIS.

Synonyms. Uncinariasis; Hook-worm Disease; Dochmiosis; Tropical Chlorosis or Anemia; Egyptian Chlorosis; Brickmaker's Anemia; Miner's Cachexia; Tunnel Anemia; Dirt-eater's Anemia; Mountain Anemia.

Definition. Ankylostomiasis is a condition of anemia dependent upon, and caused by, the presence in the human intestine of a peculiar nematoid worm, the Ankylostomum, which is present as a parasite and gives rise to anemia in its human host by its blood sucking habits, and, presumably, by the introduction into the human blood current of an elaborated toxin or substance with blood destroying properties.

Until recent years considered a tropic disease of some rarity, Ankylostomiasis is now known to be widely distributed, not only throughout the tropic belts of the world, in some countries of which it affects almost the entire population, but throughout the temperate zone as well. It equally affects males and females, regardless of race, and while far more common in early life, between the ages of three years and forty years, it may occur at any age. In many instances it is associated with a peculiar dermatitis, generally of the feet, popularly commonly known as "ground itch" and now definitely proved to be one point of entrance, or infection atrium, to the human body for the ankylostomum.

Facts of Geography and History. The wide geographic distribution of ankylostomiasis has already been indicated. Some of the countries, besides the United States, in which it has been observed and studied are Egypt, Brazil, the West India islands, Japan, the British Isles, Mexico, Italy and southern Europe, as well as a few of the northern European states, Australia, the East Indies, India, Ceylon and the Philippine Islands.

Only the modern history of ankylostomiasis is interesting, although there seem to be authentic accounts of the disease as early as the seventeenth century. The Ankylostomum duodenale was definitely discovered at Milan by Dubini, in 1838. During the latter half of the nineteenth century ankylostomiasis was discovered, described and studied in many parts of the tropic and subtropic world and, in a much more limited way, in a number of countries with temperate climates, particularly in Europe. American interest in the disease and its minute animal cause, however, practically dates from the occupation of the islands of Porto Rico and Cuba, especially the former, during the Spanish-American war. A leading medical journal recently said editorially: "If the Spanish-American war brought no other benefits in its train than those of the saving of life and suffering from yellow fever in Cuba and from uncinariasis in Porto Rico it would have been well worth the cost of men and money it occasioned. In Porto Rico the characteristic anemia, which for at least a century has been sapping the life and energy of the people, has been studied as never before, its true cause (ankylostomiasis) recognized and the proper treatment for it evolved, so that now there is a prospect that before many years have passed this evil will be eradicated." This work of eradication has been carried on so rapidly, systematically, economically and thoroughly that its accomplishment is near at hand. In 1899 Assistant Surgeon B. K. Ashford, United States Army, first reported the endemic prevalence of ankylostomiasis in Porto Rico and, appropriately enough, in recognition of his work in Porto Rico under the military regime, and particularly for his recognition of its widespread prevalence, amounting to a national curse, his services were recently besought by the government of Porto Rico and he was named to head a commission for the study and treatment of anemia in Porto Rico. The conditions met with and the methods pursued by this commission are certainly remarkable. "In valley, mountain and coast, alike, is found a ghastly population dragging out a miserable existence, and with a death rate which has shocked all who have occasion to learn of it. The number of children who have lost

parents and most of their relatives is very large, and these pick up a living as best they can. Men who should be supporting their families are chronic invalids and the families, also infected by the disease, are in a condition of misery beyond description. On the arrival of the hospital camp they came in scores and hundreds, on foot or horseback, or borne along in hammocks. They are cured, taught how to prevent reinfection and return home, well and happy, to spread the good news."

About the time of the beginning of the campaign against ankylostomiasis in Porto Rico the attention of the profession in the United States was attracted and interest in the disease was excited by the publication of the observations of Dr. C. W. Stiles, of the Bureau of Animal Industry at Washington, D.C., concerning the ankylostomum found in the United States, its distribution and the slight differences between it and the A. duodenale. From the very small number of cases of record at the time of the publication of Stiles' observations (less than twenty-five cases), the reported cases rose to more than 1000 original domestic cases and more than 100 imported cases within five years. These reported cases, however, constitute but a small fraction of the whole and there is good grounds for belief that many thousands annually acquire the disease in the United States. The medical journals continue to report groups of cases monthly, from all parts of the Union, chiefly, however, from the southeastern group of States, notably Georgia, Alabama and North Carolina and the belt long known as the "poor-white" belt, in which the residents, usually American born, have for years been adjudged shiftless, lazy and inferior, not a few of them being "dirt-eaters" (geogophasts). The astonishing discovery has been made that thousands of the "poor-whites" are the victims of ankylostomiasis, as were, doubtless, their progenitors, and that the unlovely characteristics and the low-grade mentality of these people are the symptoms and results of hook-worm disease which has long existed among them, unsuspected and untreated. That the quality of the soil, upon which our villages and farm-houses are built, is thus able to influence the characters of our citizens, by harboring and incu-

bating these parasites which rob men of their energy and life blood, is a new and amazing thought, interesting to the political economist as well as the physician. The recognition of this truth is calculated to bring public respect and appreciation to the professional sanitarian as well as co-operation and support in his remedial efforts.

Dr. George Blumer, in his oration on State Medicine before the American Medical Association, July 11, 1905, remarks that "the states in which the disease is known to be indigenous, and probably widely distributed are Virginia, North and South Carolina, Georgia, Alabama, Florida, Louisiana, Texas, Mississippi, Missouri, and Tennessee. This list includes only those in which definite evidence of the presence of the disease has been furnished; it does not include, I think, all of the infected states. Taking into account the similarities of soil and climate any one who will take the trouble to make a map of the known infected area will feel convinced that Arkansas, Indian Territory, Oklahoma, West Virginia, Kentucky and the southern portions of Illinois, Indiana and Ohio are also probably infected." * * * "Whether the disease will ever become widespread outside of its present habitat is quite another story. It must not be overlooked that a variety of circumstances are necessary to its spread; the right kind of soil, sufficient heat and enough moisture for the parasite, and a lack of certain hygienic precautions on the part of the inhabitants of the area, to be infected. The absence of any one of these conditions may be fatal to the dissemination of the disease. Considering the fact that uncinariasis has existed in the South for at least 100 years and probably longer, it does not seem very probable that it will ever extend much beyond its present limits. What is needed at present then, is a more accurate knowledge of its distribution and the inauguration of an educational and sanitary campaign to effect its extermination."

Assistant Surgeon R. P. Strong, of the Army Board for the Investigation of Tropical Diseases in the Philippines, submitted an excellent resumé of Ankytostomiasis as observed in the Philippine Islands, with a summary of the principal observations upon the

disease elsewhere, up to date, in Circular No. 1, of the First Bulletin of the Investigating Board, printed at Manila in February, 1901. His description is that of the Ankylostomum duodenale.

The so-called American hook-worm has also been encountered in the Philippines since that date, however, but whether introduced by Americans or not cannot be stated.

Etiology and Prophylaxis. An understanding of the appearance, life habits and reproduction habits of the ankylostomum is a necessary preliminary to a study of the disease which it causes. The term Uncinaria has been proposed and much used of late in place of ankylostomum, particularly by American writers, but in our discussion we will retain the term Ankylostomum which has an established cosmopolitan acceptation.

There are at least two recognized varieties of hook-worms which infest man and several others which infest cattle, sheep, dogs and other animals, producing symptoms in their hosts similar to those caused by ankylostoma in man. Of the human-infesting parasites two varieties, differing slightly in size, arrangement of teeth and oral orifices, but similar in their general morphologic features and habits, are recognized. They are designated, perhaps not wisely as evidenced by the finding of both varieties in both hemispheres, as the "old-world" worm and the "new-world" worm. Stiles applied the term Uncinaria (or Ankylostomum) Americana to the parasite which he and other workers investigated and found to be extremely prevalent in the southeastern seaboard and Gulf-bordering states of the United States.

Ankylostomum Americana is also the hook-worm most prevalent in Porto Rico and in the Panama Canal Zone. The name Necator Americana has also been proposed by Sandwith and others, for this parasite.

Worms of this variety probably cause the great majority of cases of ankylostomiasis which originate in the United States but both forms of the worm are met with in the British West Indies and there the so-called "old-world" worm preponderates. In view of the close resemblance of these worms, and the fact that their

clinical manifestations are identical, one description of the ankylostoma will suffice. It will be well to precede the description with a statement of the essential differences between the two varieties. Ankylostomum Americana is shorter than the hook-

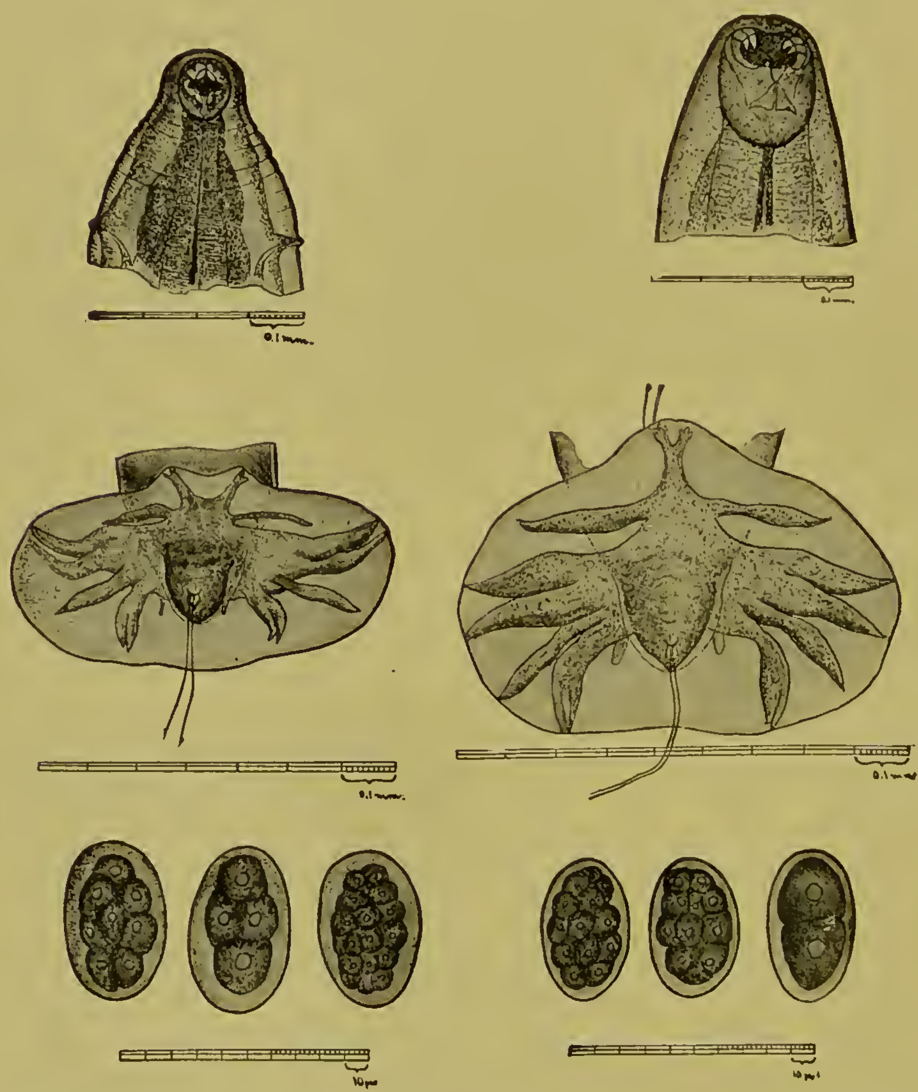


Fig. 68.—Cephalic extremities and armatures, caudal bursas and extremities of males, and eggs of two varieties of hook-worms contrasted. American worm in left column and Ankylostomum duodenale in right column.

worm which has long been known as Ankylostomum Duodenale. Its oral orifice is armed with two pairs of ventral lips and one dorsal pair with a dorsal tooth, while in Ankylostomum Duod-

enale the lips or plates are absent, the mouth being armed with six strong teeth, four of which are hooked. Within the lips of the American worm, and continuous with them, are to be made out rather delicate tooth-like structures called "lancets" and these are arranged in ventral and lateral pairs. The armature of Ankylostomum Duodenale is much more formidable than that of A. Americana. In the anatomical arrangements of their bodies the worms are very similar and this similarity extends to the eggs, which apparently differ but slightly in size, the ova of A. Americana being slightly larger than those of A. Duodenale.

In both varieties the caudal extremity of the worm terminates in a point less marked in the male than in the female. In the male there is an expanded umbrella-like bursa just above the extremity which conceals the tip of the tail and gives the caudal end of the worm a somewhat square appearance. This bursa, the "bursa-copulatrix" may be expanded or folded, being provided with ribs, and during copulation seems to fasten the male to the female. Two spicules corresponding to the penis are projected through this bursa. The worms are cylindric and the male is somewhat smaller than the female. The female measures from ten to eighteen millimeters long and the male from eight to twelve millimeters. The diameter is a little less than a millimeter. In color the worms are of a dirty white shade, and when full of blood, pink or red.

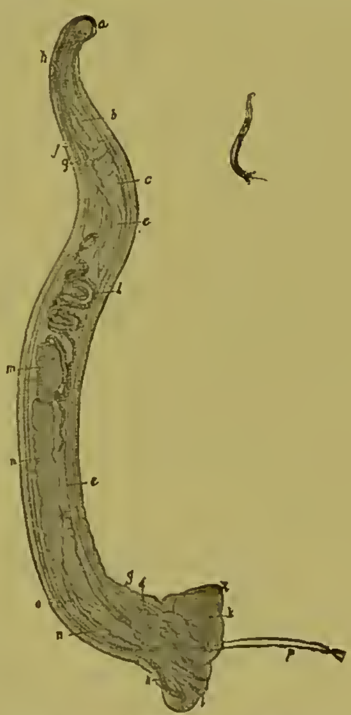


Fig. 69.—Male ankylostomum duodenale magnified and life-sized.

Briefly the life-history of this worm is as follows: Conjugation of the male and female worms occurs in the human intestine and the eggs of the impregnated female escape from the human body in the feces and are hatched in about twenty-four hours thereafter, if conditions are favorable. Warmth, air and moisture are

necessary conditions and loose, moist soil is a favorable environment for the hatching of the eggs. Growth of the embryos is rapid and accompanied by a moulting process, which is repeated several times before maturity is reached. When hatched the young rhabditiform embryo is about one-fourth of a millimeter in length and very motile. After moulting twice the embryo becomes quiescent, ceases to eat and grow and may live thus for weeks in soil or water. Gaining entrance to the human intestine by one means or another at this stage, it again casts its skin, and attaches itself to the intestinal mucosa of its host to feed, and, being sexually mature, reproduces itself. Conjugation of male and female worms and reproduction may take place outside of the body (according to Giles, Sandwith and others), after sexual maturity is attained.

There is no evidence that an intermediate host is necessary in the life cycle of the ankylostomum.

The body in both male and female worms tapers towards the neck, which is so bent upon the body that the oral orifice presents on the dorsal side of the worm. In the human intestine the females usually outnumber the males. Sexual productivity of the females lessens with age, and the adult life of the hook-worm has been shown to be a long one, probably several years. Loos states that acid fermentation in the intestine will kill all eggs and larvæ.

The fact that the hook-worm gains entrance to the bodies of men and animals by penetrating the skin was discovered by Loos in 1894, but it was not until 1904, ten years later, that the route, by which the embryo, gaining entrance in this way, reaches the intestine, was demonstrated by the discoverer. In the meantime, however, abundant evidence in proof of this method of infection was accumulated by other observers and in the United States evidence was collected which not only confirmed Loos' claim but indicated that transdermal infection is even more common than direct infection by ingestion. In North Carolina and elsewhere in the United States, "ground-itch," which is probably the skin lesion caused by concentrated earth cultures of anky-

lostoma embryos, goes hand in hand with ankylostomiasis. The principal American investigators of Ankylostomiasis during the last half decade are Stiles, A. J. Smith of Philadelphia, Claude A. Smith of Atlanta, Nicholson and Rankin, Harris and Bondurant and the Army medical workers referred to. In 1904, and again in 1905, Claude Smith reported before the American Medical Association cases of experimental infection with ankylostoma through the skin, with subsequent development within the intestine of the human subject, and recovery therefrom, of adult worms. In the 1905 report all sources of possible error or accidental direct infection by ingestion were carefully controlled and eliminated, and 1348 ankylostoma, 752 females and 596 males, were recovered from the infected individual. Smith's experiment consisted in the application of a highly concentrated earth culture of ankylostoma larvæ to the arm of his subject with the immediate production of the "ground-itch" lesion, redness, vesicles, crusts and swelling of the tissues, intolerable itching and some constitutional disturbance. In six weeks ova were present in the stools and eight weeks later hook-worms to the number of 1348 were recovered, after an anthelmintic was administered. Smith found the age at which the larvæ penetrate the skin to be from four to eight days. His experiments confirm beyond the possibility of question the observations of Loos in 1894. The discovery by Loos was an accidental one. By noting the irritation caused by a drop of water containing (approximately) 1000 embryos, which fell upon his hand, the disappearance of the embryos into the skin, leaving their tiny shells behind them, and the subsequent development of intestinal ankylostoma in himself, he was led to experiment upon both animals and men, establishing the truth of his observation by repeated studies upon puppies and human beings. Captious critics, however, attempted to discredit Loos' observations and raised objections on the ground of imperfect exclusion of ingestion infection. These objections are definitely overcome by the careful confirmatory experiments of Claude Smith (Journal of the American Medical Association, October, 1905).

Loos' crowning achievement in his studies of ankylostomiasis was

the demonstration in 1904, after ten years' work, of the route by which ankylostoma embryos, penetrating the skin, find their way into the intestine of the host. Loos' puppy experiments show conclusively that the route, briefly, is as follows:

The mature larvæ bore into the skin, using the hair follicles as gates of entry and leaving their sheaths or shells behind them. It is established that the degree of irritation produced is dependent upon the number of larvæ. Through the hair follicles they reach the lymph spaces, lymph vessels and glands and at length, by way of the thoracic duct, the veins; thence to the right heart and the blood vessels of the lungs where they easily penetrate to the air cells. Gaining the bronchial tubes, trachea and larynx they reach the mucosa of the digestive tract and the journey via the esophagus and stomach to the small intestine is then an easy one. Once the mucous membrane is attained the larvæ (in the presence of air) continue to develop and this development is completed in the intestine.

Recognizing two distinct and principal methods of infection our *Prophylactic* efforts should be directed against them. To prevent ingestion infection, which means the taking into the intestine, via the mouth and stomach, of young ankylostoma embryos, we should enjoin the filtration and boiling of all drinking water, the thorough washing with boiled water of all vegetables eaten raw, or better, the cooking of all vegetables; the prevention of the deposition of feces upon soil in which vegetables are grown and the medical treatment of all cases of ankylostomiasis, to prevent the passing of ova into the air, soil, and moisture necessary for their development. An interesting and fortunate circumstance is the inability of the ovum (except under most unusual conditions) to hatch within the intestine. Thus, when the original parent worms are destroyed in the intestine the patient will be free from infection unless he incurs a reinfection by ingestion or through the skin.

The second infection method, through the skin, may be almost certainly avoided by all persons who are not earth workers by wearing shoes, and in the case of earth workers, by wearing gloves

also. Infested soil may often be rendered safe by turf fires, ploughing and exposure of the soil to the sun. Mine workers and tunnel diggers will scarcely be protected by these devices, however, and the greatest safeguard lies in proper latrines, or the disinfection of all stools. Manifestly, the persons hardest to reach are the ignorant, superstitious and uninstructed natives of tropic countries. Concerning the prevalence of ankylostomiasis, amebic dysentery, and similar infections in Egypt and the habits of the natives, Sandwith remarks that "the fellaheen unconsciously devote their lives to encouraging their entazoa," a statement equally true of the Filipinos and of less civilized tropic dwellers, who disregard all sanitary laws in the disposal of their excreta.

In education and enforced sanitation, especially with regard to the promiscuous deposition of feces in the vicinity of huts and houses and gardens, lie the hopes of eradicating the disease among the natives of hot countries.

Manouvriez advocates the flushing and irrigating of mines with a solution of salt, of a strength of two percent., or the scattering about of loose salt, as an inexpensive method of destroying larvæ in and about the mines. He bases this suggestion upon observations in mines where these conditions occur naturally and where, as he claims, ankylostoma infestation does not occur.

Pathology and Diagnosis. The pathologic anatomy, as observed in the body recently dead of ankylostomum anemia, presents a few distinctive features, most prominent of which is the condition of the *small intestine* which also shows, still in an attached condition in the case of recent death, the hook-worms. The number of the ankylostoma may vary from one to a thousand or more, although it is inconceivable that a single worm would ever cause the death of its host. The pathologic manifestations of concurrent diseases must be carefully separated from those of ankylostomiasis. The small intestine in its upper portion is bathed in mucus, which is found to be mixed with blood lower down in the intestine. When the mucous exudate is removed the intestinal mucosa shows islands of swelling and injection with many ecchymoses. The hook-worms, if still present, hang from the intes-

tinal wall, their heads often buried in the mucosa, so firmly fastened as to resist washing or brushing away. They are found, when present, in the lower duodenum, jejunum and upper ileum, only. An intestinal catarrh proportionate to the number of worms present (or indicated by scars and lesions) will usually be noted. Microscopically, a torn condition of the villi at the site of attachment of the worm will appear, or there may even be complete destruction of the entire villus. Infiltration of all the coats of the intestine down to the serous coat, with small round cells, blood cells, both red and white, particularly eosinophiles and polymorphonuclear leucocytes, will also appear.

The eggs of the hook-worm are not found in the mucosal tissues, either encysted or otherwise, but an occasional loose ovum is seen free in the intestine. The hook-worm may actually penetrate the mucosa, passing into the submucosal tissues, and blood filled cavities beneath the mucosa, containing one or two worms, have been found postmortem.

Loos maintains that the ankylostomum is not merely a blood-sucker but that it feeds upon the tissues of the mucosa, actually eating them. The *colon* presents a normal appearance except for a pale color.

All the tissues and organs of the body contain reduced amounts of blood and are pale in color in severe cases. In addition to this there are to be noted effusions into the pericardium and into the abdominal cavity. The *kidneys* are apt to be large and pale and to show fatty degeneration throughout. The capsule strips easily from the organ.

The *liver* likewise shows fatty degeneration and in addition, in some cases, a yellow pigmentation, the origin of which is uncertain. The pigment granules are found deposited within the liver cells and give the chemical reaction for hematoidin, but the occurrence is not constant. The *heart* and blood vessel walls share in the degenerative process, which is in reality widespread throughout the body, being of the character noted in cases of severe anemia from other causes. The question of toxins, derived directly from the parasites, in connection with the production of

these degenerative changes is unsettled. It is entirely possible that such toxins exist and that intestinal toxemia also plays a part, but the proof of both propositions is wanting. There is likewise no proof that hemolytic toxins are present in the blood in ankylostomiasis and there is some weight of authority to indicate that the anemia is simply the result of blood abstraction, but the Japanese observers adhere to the toxic theory of causation for the anemia. In kind, the anemia may approach that of the pernicious progressive variety; on the other hand, it may be trifling, in the presence of a slight infection. In severe cases there is not only a reduction in numbers and hemoglobin values of the erythrocytes, but poikilocytosis, and the presence of microcytes and megaloblasts and nucleated red cells, are to be noted. Absolute leucocytosis may be present but is not the rule, but eosinophilia, ranging from five to eight, and even to forty percent. of the total leucocytes, is rather constantly noted and constitutes a diagnostic clue of some value. The *spleen* shows no constant nor characteristic changes.

The *heart* is dilated and flabby.

The *brain* is unusually white.

The *skin* is pallid or lemon-yellow in color, the shade varying with the race of the subject and the degree of anemia.

The bodies are usually plump, rather than wasted, an appearance emphasized by the presence of dropsical edema.

Diagnosis. The diagnosis of ankylostomiasis from purely objective symptoms (exclusive of the detection of worms or ova in the stools) is not always possible, even in regions where the disease is known to be prevalent. Anemia, especially in the tropics, is apt to be due to chronic malarial disease or to other infectious conditions. However, a history of previous ill-defined lesions of the skin of the feet, "ground-itch," occurring in an anemic individual leading a bare-footed, outdoor life, constitutes strong presumptive evidence of hook-worm infection, and anemia in earth workers generally should at once suggest the possibility of ankylostomiasis. Careless or filthy habits of living and of disposing of human excreta constitute grounds for suspicion. Under these circumstances a *therapeutic diagnosis* is possible. It consists

in an anthelmintic dose which will cause the hook-worms, if present, to appear in the stools where they are visible to the naked eye, upon careful inspection. For the detection of eggs a microscope is essential. In view of the possibility of overlooking a few worms in the stools, and of the great number of eggs present and discoverable with a low power objective, the microscopic method is the most reliable. A dram (4 cc.) or more of the feces should be diluted with filtered water and centrifugated or permitted to stand in a conical glass. A drop of the upper part of the sediment will contain the ova, if present.

The ova are so characteristic that they are not apt to be mistaken for those of other parasites. Ankylostoma ova do not show the bile staining present in so many other parasitic eggs found in human feces. The egg is clear, with a granular gray content showing through the shell, divided into four, six or eight equal parts. If ankylostomiasis be accompanied by fever of intermittent or continuous type a blood examination for malaria hemamebas should be made to clear up the cause of its occurrence. Such fever may occur as a symptom of ankylostomiasis without concurrent malarial infection. The noneffectiveness of quinine upon the temperature will usually serve to exclude malarial fever if a question of diagnosis arises. Mild cases of ankylostomiasis are apt to be mistaken, on superficial examination, for digestive diseases and in more severe cases for kidney and heart diseases.

Concerning the diagnostic value of "ground-itch" in connection with ankylostomiasis, Sandwith, in Egypt, finds it extremely common, and Nicholson and Rankin, in the United States, report that over 99 percent. of 150 cases studied by them gave histories of "ground-itch" and in 69 out of 90 cases the "ground-itch" certainly preceded the occurrence of other symptoms. (Medical News, Nov. 19, 1904.) Eosinophilia, while common in other parasitic infections, is suggestive of hook-worm infection when noted in association with anemia. Boycott, (according to a London letter in the Journal of the American Medical Association, in 1904) states in an English government report that a percentage of eosinophiles exceeding five percent. of the total leucocytes

suggests a probability of ankylostoma infection, increasing proportionately with the increasing percentage of eosinophiles. His observations were made among mine workers.

Beriberi and ankylostomiasis present some common symptoms but the anemia of beriberi is insignificant as compared with ankylostomiasis anemia. Effusions are common in both diseases but there should be little difficulty in discriminating between the two affections. The neuritic and paretic symptoms of beriberi do not occur in ankylostomiasis.

From parenchymatous nephritis, to which ankylostomiasis bears some clinical resemblance, it may be distinguished by the anemia and by the presence of ova and parasites in the stools.

Symptoms and Treatment. In studying the symptomatology of ankylostomiasis we will do well to divide our cases into two classes, the acute cases and the chronic cases, although no arbitrary time can be fixed at which an acute case becomes chronic. Both classes will include mild and severe forms with intermediate degrees of severity. A mild acute case may become, in time, a severe chronic case. As has been previously pointed out, the hook-worms do not multiply within the intestine and an infected person removed from the environment and conditions favorable to continued reinfection may simply harbor the original infecting worms. Thus it will be apparent that the severity of the anemia will usually depend upon the number of hook-worms and the length of time they have been present in the intestine in any given case. It is believed that the local effects of Ankylostomum duodenale are more severe than those of Ankylostomum Americana, and that a smaller number of the "old-world" worms are required to produce severe symptoms. The greater size of this hook-worm, and its consequent ability to abstract more blood, and the more severe wounding of the mucosa caused by its powerful hooks, are offered as reasons for this belief.

A. J. Smith (International Clinics, Vol. II, Series 14) suggests, from his own experience, that infections with from 50 to 300 of the American ankylostoma probably gives rise to mild or moderate symptoms and that from 300 to 1000 or more hook-worms will

probably produce severe symptoms in an adult host free from other diseases. These numbers should be reduced for the ankylostoma duodenale.

Most of the symptoms may be referred to the digestive, circulatory and nervous systems. In slight infections the symptoms may be absent or so trifling as to be overlooked.

In *Mild Acute* cases there may be epigastric uneasiness or even pain, and variability of the appetite. The pain may be relieved by taking food or it may be increased thereby. Dizziness and frontal headache may be present and languor, either physical or mental, sets in early. The circulatory symptoms are palpitation and shortness of breath and the subject begins to show pallor of the skin. Arrest of development from impaired nutrition is very apt to occur in children. The feces do not show the presence of blood.

In the *Moderate Acute* case these symptoms are accentuated in direct proportion to the degree of anemia. Thus, in addition to a capricious and failing appetite there may be a morbid craving for dirt, earth or sand, (geophagy) especially in children. The digestive symptoms may now include nausea and vomiting. The headache and dizziness are severe and tinnitus is also present. Fever of irregular type or with quotidian exacerbations may be present, or a subnormal temperature may be constant. The palpitation is now marked and slight arthralgias may be complained of. Pallor of the skin, buccal mucous membranes and conjunctivæ, is well marked. Blood, either occult or visible, may be recognized in the feces.

The picture of *Chronic Mild* ankylostomiasis may be simply the picture of the acute mild form of the disease protracted, the balance between the destructive and constructive or reparative process never being entirely lost. The subject is a moderately anemic individual with minus activity of nutritional, mental and physical functions and faculties. Such cases if untreated may exist for years.

The *Advanced Chronic* cases, the truly severe forms of ankylostomiasis, are secondary to the acute moderate cases described

and the patient shows intense anemia and pallor with pearly, slightly icteric scleræ, dryness of the skin, clubbed finger-tips which show cyanosis, and many of the evidences of innutrition and oxygen starvation.

The digestive symptoms are either very pronounced or absent. There may be vomiting upon the ingestion of food or there may be fairly good digestion with no discomfort attendant upon it. The feces may contain visible blood and the bowels may be loose or constipated. The pulse is weak, soft and compressible but not usually rapid except upon exertion, when palpitation and dyspnea occur. At the apex and at the base of the heart and over the large veins of the neck are to be heard hemic murmurs and moderate dilatation of the heart can be made out. Tinnitus and vertigo, and dim vision with dilated pupils are present and the urine, while generally free from albumin and casts may contain them, the kidneys during this time undergoing degeneration. Sleepiness and impotence were observed as decided symptoms, in many cases in Egypt, by Sandwith.

The ankles and feet show swelling, and ascites and general anasarca may develop, with effusions into the pleural and pericardial sacs.

These clinical groupings must not be taken as absolute ones; the disease does not permit of a sharply defined classification and the acute cases gradually fade into chronic ones.

Another acute class of cases has been described in which the onset is similar to that of acute dysentery. The initial symptoms are those of gastro-enteritis, vomiting and diarrhea with blood-stained feces. After the subsidence of the severe acute symptoms, which are probably due to the simultaneous development and attachment within the small intestine of a large number of ankylostoma, these cases take on the characteristics of the less suddenly developed severe infections.

Concerning the disease generally, irrespective of the clinical grouping suggested, abdominal soreness or discomfort, especially in the upper abdomen, is frequently complained of and diarrhea may be troublesome, although constipation is rather common

in ankylostomiasis. Both gastric and duodenal catarrh are apt to be present and cholecystitis is observed occasionally. In children the abdominal symptoms are common and it is not improbable that the presence of hook-worms even gives rise to convulsions in the very young. Liver enlargement is rather commonly observed. The nails early show the effects of poor nutrition, becoming furrowed and brittle. The skin becomes harsh and dry and general pruritus is observed. Loss of flesh is not notable except in advanced cases. As in other forms of anemia, dangerous or fatal hemorrhage is apt to occur. Pigmentation of the tongue and lips and also of the skin has been observed in a large number of cases but is much less common in Caucasians. It should be remembered that this condition is a common accompaniment of malarial disease and that a large portion of the natives in tropic countries are malarial subjects.

It is also probable that the vicarious distribution of pigment in the dark skinned races often occurs in the absence of disease. Disturbed innervation and hemoglobin disintegration due to toxins, have been proposed in explanation of this pigmentation.

A. J. Smith observed that cases of intractable malarial cachexia, in the United States, associated with ankylostomiasis, were far more amenable to treatment after hook-worms had been expelled.

We can perhaps gain a better idea of the clinic character of "*ground-itch*" from a study of the experimentally produced cases. This affection, consisting of localized inflammatory eruptive skin lesions, is caused by the direct action of ankylostoma larvæ at the point at which they enter the skin. Various native names are given to this condition but among English speaking peoples generally it is known as "ground-itch" or "water-itch." As it ordinarily occurs, suppuration is usually present and this is probably not dependent upon the ankylostoma larvæ but upon associated pyogenic bacterial infection. In experimental cases suppuration is not conspicuous. Intense redness and swelling first appear, and vesicles, which soon become confluent, forming larger blebs, promptly develop. If pus bacteria are present the contents of the blebs will be purulent in character. The

itching and burning are intense and there is considerable inflammatory reaction in the surrounding tissues. When the vesicles or blebs rupture, crusts form and after a few days these crusts are cast off as scales. The "ground-itch" lesions usually appear about the feet or ankles and occasionally about the hands and wrists. In Claude Smith's experimental cases the skin was protected from scratching by plain gauze bandages. Owing to the extreme concentration of the earth-cultures of ankylostoma larvæ used, the reaction was probably more than usually violent in his experimental cases. In naturally acquired cases of "ground-itch," where the subject is permitted to scratch the lesions with his nails, suppuration will almost certainly be added to the inflammatory process and chronic ulceration and considerable destruction of tissue may supervene.

Treatment. In view of the cosmopolitan character of this disease, its widespread distribution and its serious consequences, both to the individual sufferer and to the community, it must be accounted fortunate that we have a specific cure for ankylostomiasis. In view of what has been stated it will be plain that but two indications as to treatment exist; first, to dislodge and remove the hook-worms from the intestine of the host, and, secondly, to repair the damage which they have done, or in other words, to correct the condition of anemia. The prophylactic treatment has already been considered.

The first indication as to treatment is the more important one, as the great majority of patients when freed from the hook-worms get well with little or no medical treatment. Exceptionally, severe cases may die in spite of the removal of the cause of the anemia. In individuals in whom the hemoglobin has been diminished to a very low percentage and the cellular elements of the blood are much reduced numerically, in short, in such cases as present pernicious anemic symptoms, the eviction of the hook-worms may come too late to save life. Fortunately these cases are comparatively few. The Porto Rico commission found that nearly all cases get well without anti-anemic treatment after the worms are expelled.

Naturally, blood reintegration and repair is hastened by the exhibition of hematinic drugs but these are not imperatively essential in most cases. The measures directed to expel the worms are purely medical.

After appropriate preparation of the patient's alimentary tract, by dieting and purgation, the chief object of which is the expulsion of protecting masses of feces and mucus, the chosen anthelmintic may be given and in most cases the cure will be effected within a few days. Some refractory cases are encountered and Norsa, speaking, no doubt, of infection with the ankylostomum duodenale in Italy, remarks that the cure of this condition is liable to be far from an easy matter, and suggests that, in the event of failure of the usual anthelmintics, others be tried. The consensus of opinion concerning the choice of a drug, among American physicians, whose experience has been chiefly with ankylostomum Americana, is in harmony with that of the leading European, Egyptian, East Indian and Japanese observers who have dealt chiefly with the ankylostomum duodenale. There is a general agreement that *thymol* is the most effective drug for expelling hook-worms. All, likewise, agree that the drug is a somewhat dangerous one, particularly in feeble subjects, and that certain precautions are necessary in its use. The drug is given undissolved and in large doses, with the expectation that slow and incomplete solution within the intestine will kill the hook-worms and that subsequent cathartic drugs will remove the worms and the undissolved thymol, before poisonous effects from absorption of the drug have time to occur. The plan may well be criticized as a clumsy one and it is to be hoped that some harmless or less dangerous drug will prove as efficacious as thymol. The principal precaution necessary is to see that no solvents of thymol are given before, during, or after the use of the drug. *Oils* and *alcohol* are solvent for thymol and both *must be avoided* in every form. Ether, chloroform, solutions of chloral and alkalies, are also solvent for thymol. Wines or spirituous liquors and olive oil may not be taken and no drink but plain water should be permitted.

Results from the use of thymol have been so satisfactory, however, that it is at present the most generally employed anthelmintic in the treatment of ankylostomiasis.

Sulphate of Magnesium is the favorite cathartic for use in combination with thymol and it is claimed that it is somewhat antidotal to the thymol. The plan followed by the physicians of the Anemia Commission in Porto Rico is substantially as follows: The evening meal is omitted and a full dose of an ounce (31 grams) of magnesium sulphate is administered at bed time. In the morning, the magnesium sulphate having meanwhile produced free watery movements, a dose of 30 grains (2 grams) of thymol is given at 7 A. M., the patient remaining in bed without breakfast. (Six capsules of 5 grains each may be given.) At 8 A. M. the dose of thymol is repeated, in the same amount, and two or three hours later another dose of magnesium sulphate (one ounce) is administered. It is claimed that the Epsom salts effectually checks absorption, as well as flushing out the intestinal contents.

Some American physicians give three doses of thymol, of 2 grams each, or ninety grains in all, at intervals of an hour before administering the expelling dose of Magnesium Sulphate. All of the above mentioned doses are adult doses. To children the thymol may be given in doses of from 5 to 15 grains at a dose, according to the age and the degree of strength of the individual. It is highly important that the physician be familiar with the *symptoms of thymol poisoning* and also with the *treatment.* The symptoms are those of paralyzed nerve centers in the spinal cord and medulla, lessened reflex action, slowed respiration, lowered temperature and arterial tension, and general weakness and coma, which usually precedes death. A sense of warmth in the epigastrium, ringing in the ears, the sensation of constriction about the head and an increased output of urine, greenish in color, indicate absorption of the drug. The treatment should include stimulation, by needle, with nitroglycerine, strychnine or atropine, external heat and free purgation with the sulphates of magnesium or sodium. Emesis, or preferably, lavage of the stomach should be employed to remove any thymol remaining in that organ.

The utmost care should be employed to prevent attendants or friends from administering alcohol or other solvents in any form.

A number of other drugs have been used and advocated for expelling hook-worms. Most prominent among them is male fern, a drug less toxic in its action than thymol and also less effective, for this particular worm, according to a number of observers. It may be given in four doses of one gram each, of the oleoresin, at intervals of one-half hour, observing the same rules as to preparations of the patient advised for the use of thymol, viz., as to the preparatory purgation, dieting, and administering the drug in the morning, when the stomach and intestine are empty. One hour after the last dose of male fern is given the expelling purgative, consisting of magnesium sulphate (31 grams), or two drops of croton oil dropped upon loaf sugar and administered fractionally every ten minutes until free catharsis results, should be given.

Neumann claims from experience and experiment that podophyllin prevents ankylostoma from clinging to the intestinal mucosa and advises that male fern administration be preceded by the administration of podophyllin.

Calomel is also used as a preparatory purgative.

A mixture of two grams of sulphur, half a gram of terpin and two grams of condurango, is claimed by its advocates to be a perfectly safe and invariably effective anthelmintic dose.

In a large series of hospital treated cases observed by Sandwith, in Egypt, he found the *mortality* to be eight percent. Of the total number of the cases treated 89.5 percent. were cured or much relieved and the remaining 2.5 percent. were unrelieved. From his description it is believed that the cases, as a whole, came from a class much inferior to that in which the disease occurs in America or Porto Rico but probably very similar in habits and manner of life to the lower class Filipinos. He states that in Egypt the patients apply for treatment after reaching the most distressing stages of anemia and after such barbaric and superstitious attempts at self-treatment as cauterization with red-hot nails or the wearing of setons in the epigastrium.

DETECTION OF THE PARASITE.

Whatever the drug or combination used, it should be followed by free purgation, preferably with salines, to expel the hook-worms. All the stools for twenty-four hours should be strained and washed through a cheese-cloth sieve. The mucus may be dissolved by the addition of liquor potassa and the contents of the cheese-cloth then placed in clear water and the worms picked out and counted. At the end of the week the stools should again be examined for ankylostoma ova. If after several examinations these be not discovered a cure may be pronounced. If on the other hand the infection is shown to persist, the treatment should be repeated.

CHAPTER II.

FILARIASIS.

Synonym. Filariosis.

While the term Filariasis as applied to man would, if strictly interpreted, include dracontiasis (Guinea-worm disease), elsewhere described, and certain filarial infections occasionally found in the conjunctiva (f. loa), the bronchi (f. bronchialis), and the mouth (f. hominis oris), as used here it refers solely to human infection with certain nematode worms which inhabit the blood and lymph vessels, both in their adult and embryo forms, and give rise to a group of affections known as "filarial diseases," commonly encountered in many tropical countries.

Filariosis has been suggested as a more appropriate name for the condition of filaria infection. The entire subject is one concerning which our information is incomplete and somewhat fragmentary, and it is difficult to set forth simply, plainly and connectedly, the determined facts concerning human filariasis. The term *filaria sanguinis hominis* includes the embryo phases of at least three different species of filarial worms, much alike in their general size and appearance, but differing in their periodicity and constancy of occurrence in peripheral human blood, and taking from these peculiarities distinguishing names: *Filaria sanguinis hominis diurna*, *f. s. h. nocturna*, and *f. s. h. perstans*, the day, night, and constant worms, respectively. These three varieties of embryo worms all have, presumably, corresponding adult or parent forms too large to circulate in the blood or lymph stream, and found, therefore, in groups in the lymphatic trunks. This is known to be true for one variety, *f. s. h. nocturna*, the parental form of which worm is found in the lymphatic trunks in pairs (males and females), and in groups of six or more, and is known as filaria Bancrofti. Our information concerning f. s. h.

nocturna, and its parent, f. Bancrofti, is more complete than in the case of the other varieties of filariæ. It would be far better to speak of the adult and embryo forms than to multiply terms; for example, *adult* f. s. h. nocturna rather than f. s. h. Brancrofti. Our more complete knowledge of this parasite, filaria nocturna, embryo and parent, is due in great part to its widespread distribution and to the fact that it alone, so far as known at present, is identified in a causal way with the filarial diseases. As our discussion of human filariæ is preliminary to consideration of these diseases we will take this filarial worm as a type and follow its life-history in man.

Before doing so, however, we may state the **Geographic Distribution** of the parasite which corresponds, of course, with the distribution of filarial diseases.

In the tropic and subtropic belts, both south and north of the equator, it is found in nearly every country of the globe, varying greatly, however, in prevalence. Thus, while rare in the United States, it is exceedingly common in the Samoan and other Pacific Islands, in China, India, and Africa. It is less common in the West Indies, Central America and the Philippines, but, it is never extremely rare in any of these countries.

The embryo filaria sanguinis hominis nocturna is of about the thickness of the diameter of a red corpuscle 0.0075 mm.—(average about $\frac{1}{3200}$ of an inch) and measures about 0.2 to 0.3 mm. in length (average $\frac{1}{80}$ of an inch). It is transparent and colorless and is actively motile, possessing a thrashing movement, coiling and uncoiling itself like a snake and causing great displacement of the red blood cells. The embryo has a sharp tail-like extremity and a rounded head with an ill-defined, six-lipped armature, best seen when the motility of the parasite has about ceased. The embryo worm is enclosed in a loose, transparent sheath somewhat longer than the worm but generally conforming in shape to its body. Within this loose sheath, the worm moves freely, permitting the unoccupied and collapsed portion to protrude before the head, or to drag after the tail, or both. Other distinguishable features about the embryo are two luminous

triangular points of doubtful significance, one perhaps $\frac{1}{300}$ of an inch distant from the head of the worm, the other somewhat nearer the tail, and a fine, cellular structure marked by circularly placed striations, best made out in stained specimens. The adult parasite resembles a transparent horse hair in its gross appearance. Both males and females are recognized, the female specimen being longer and thicker then the male and containing a double uterine tube, filled with embryos. Vaginal and anal orifices are to be made out. The males and females are coiled closely together in pairs, or in groups of six or eight.

If the peripheral blood of the human host be examined with a $\frac{1}{4}$ inch or even a $\frac{2}{3}$ inch objective at the appropriate time, the

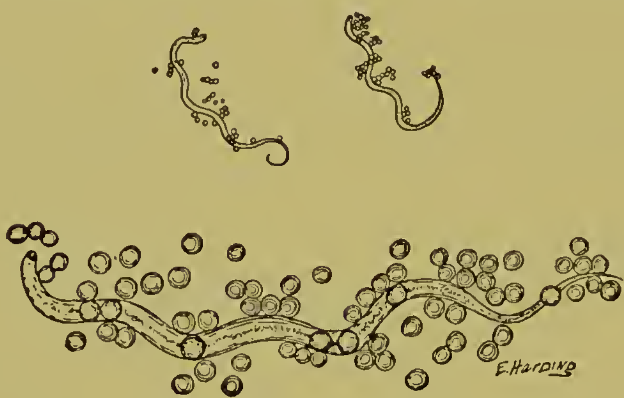


Fig. 70.—Filaria sanguinis hominis and red blood cells. Upper magnification with $\frac{2}{3}$ inch objective. Lower magnification with $\frac{1}{4}$ inch objective. (From Coplin.)

embryos may be found in a drop of blood to the number of 300 or even 400. While the causes of this periodic appearance in the peripheral blood, and disappearance from it, have not been satisfactorily explained, the facts are undisputed, and it has also been shown (postmortem) that when absent from the peripheral circulation the embryos are present in enormous numbers, many hundreds to each drop of blood, in the blood vessels of the lungs and in the aorta, and that none are present in the liver and spleen. Why these embryos should thus migrate from the periphery to the true centre of the circulatory system, the lungs and heart, at stated hours and with clock-like regularity, is a problem which remains to be solved.

Filaria nocturna is *convertible into a day parasite* (in its peripheral appearance) by causing the sleeping habits of the host to change from night to day, but the same conversion does not hold good for filaria diurna, which remains diurnal in its peripheral appearance whether the host sleeps by day or night.

As previously stated, *filaria perstans* can be detected by day or night. In both embryo and adult forms f. perstans differs from f. nocturna; and f. diurna differs in both size and appearance, the embryo being shorter, more elastic, and without a sheath, and being possessed of greater progressive motility. The adult resembles the adult filaria nocturna rather closely, the males and females being distinguishable.

In order to follow the life-history of the embryo filaria, we must observe it in its *intermediate host*, the *mosquito*, whereby it is abstracted from the peripheral blood of man to undergo within the insect a definite growth and development and then to be again introduced into man through the insect's bite; to find its way into lymphatic trunks, undergo sexual mating and reproduction, the embryos passing into the blood current, while the parent filariæ, male and female, remain fixed in the lymphatic trunks.

This wonderful extra-human existence of the parasite is observable in every stage of the mosquito from the time of its abstraction from the human blood to the time of re-introduction to man at the instant of the insect's bite. A brief statement, only, of the various occurrences which take place within the mosquito can be given here.

The particular variety of mosquito most concerned in filaria distribution is *culex fatigans*, an extremely common variety in most tropical countries. It is possibly also distributed by one or more of the anophelina. Sucked with the meal of blood into the stomach, or mid-gut, of the insect, the embryo filaria there makes its escape from the retaining sheath. This phenomenon (ecdysis) is caused, it is supposed, by an increased viscidity in the blood due to its digestion in the insect's stomach. The filaria violently bursts from its sheath and is then at liberty to penetrate the tissues of its intermediate host, which it is prevented

from doing in the human (definitive) host by its sheath or envelope. In the next stage we find the escaped filariæ among the thorax muscles of the mosquito where they become passive and remain for two weeks or more undergoing a development which brings them to a size of $\frac{1}{16}$ of an inch in length (an increase of 500 percent.) and provides each with a digestive canal and mouth and a vigorous activity which is put forth in wandering about within the insect, reaching all of its tissues and penetrating the hollow proboscis, sometimes in pairs, thence to be re-introduced to man during the mosquito's first meal of blood.

This, in brief, covers the intramosquito life of filaria nocturna. Many details of interest and importance from the viewpoint of the student are necessarily omitted here, and we are brought back with the parasite to the *definitive host, man*, to study its part in the production of the clinical conditions known as filarial diseases.

Fortunately in the great majority of cases the condition of filariasis is an innocent one, producing no evil effects whatever, so far as can be observed. The extreme prevalence of the infection in the inhabitants of certain endemic areas in tropical countries, (from ten to fifty percent. of the population being hosts of filaria nocturna) makes the fact of benignity one to be thankful for. The percentage of cases of filaria infection which do develop disease conditions therefrom, can only be surmised. The presence of embryos in the peripheral blood is productive of no evil, so far as known, but the presence of the adult worms, each measuring three or four inches in length, and often occurring in bundles and coils of six or more, frequently produces mechanical obstruction of the lymphatic canals, which causes lymph stasis, edema, varicosity, inflammation and thickening of the vessels, and even abscess, either from the death of the adult worm, or from an implanted pus infection.

The tropical *elephantoid diseases*, so called, are generally, if not invariably, expressions of lymphatic obstruction from filarial worms or ova. They include elephantiasis of the legs, scrotum, arms, external female genitals, scalp, and localized skin areas.

These conditions are preceded by filarial lymphatic varix, lymph stasis and inflammation of the lymphatic vessels (the latter occurrence being considered essential in the causation of true elephantiasis), and hyperplasia of the connective tissues.

The premature escape of filaria ova (not embryos) incapable of progressing through lymph glands, but capable of causing embolism in these glands, is supposed to play a part in producing lymph stasis. Manson's theory of the causation of elephantiasis is based on the finding of filaria ova in lymph from lymph scrotum and lymph varix cases. The sequence of events suggested by him as explaining the production of elephantiasis by filaria, is as follows (page 572, Tropical Diseases): "Parent female filaria in the lymphatic stream of the affected part; injury of the filaria; premature expulsion of ova in consequence of injury; embolism of lymphatic glands by ova; stasis of lymph; lymphangitis from subsequent traumatism, or other cause (septic infection) in the congested area; imperfect absorption of the products of inflammation; recurring attacks of inflammation leading to gradual, intermittently progressive inflammatory hypertrophy of the part."

By this hypothesis, Manson explains not only the production of elephantiasis, but the clinical fact that filaria embryos are generally absent in cases of elephantiasis; assuming that the parent worm, which gave rise to the obstruction, was injured and aborted, and whose escaped ova produced the lymph stasis, died during the early stages of the disease.

Elephantoid fever is probably a symptom of lymphangitis and accompanies the swelling, pain, and redness of this condition. If it takes on a septic type it is suggestive of abscess of lymphatic glands, and if the pain is located deep in the belly the concealed intraabdominal lymphatics may prove to be affected and call for abdominal section. A previous history of filaria infection, and other expressions of the same, would make the suspicion of intraabdominal lymphatic abscess stronger.

When elephantoid fever is nonseptic in character it lasts for several days and generally ends critically, often with a critical sweat or a critical discharge of lymph through the skin. The

fever is apt to recur and may be mistaken for a malarial expression. It may, of course, occur in a person with both filaria and malaria infections, but should be recognized on account of its association with anatomic changes in the lymphatic system. The **Diagnosis** of elephantiasis by gross manifestations should be easy. The same may be said of varicose inguinal glands, lymph scrotum, chylocele, and chyluria, other pathogenic manifestations of filarial obstruction of the lymphatic system. If the thoracic duct be obstructed by adult parasites the chyle finds its way backward, dilating the lymphatic vessels to enormous dimensions, the pelvic and abdominal lymph vessels becoming one enormous intercommunicating varicosity. Whenever the various superficial lymphatics become prominent, we have a varicose tumor, as in the scrotum and the glands of the groin, axillæ, etc. If chyle escapes into the bladder from ruptured, distended lymph vessels, or into the kidney from the same cause, it appears in the urine (chyluria) and when it escapes into the tunics of the testes we have the condition of chylocele. Puncture of the prominent varicosities at any point will cause an outpouring of chyle and will establish a diagnosis, the embryo filaria being present unless the disease is advanced and the parent worm dead. These occurrences are generally painless at first, and remain so, until lymphangitis sets in. The skin is not adherent to the varicose tumor. Groin varicosities may have to be differentiated from buboes and hernias but they should present no difficulty. Puncture should not be performed if doubt exists.

Surgical treatment has a limited application and is not advisable unless the tumors cause pain and disability. In case surgical relief, excision, be attempted, the ligations of lymph vessels should be as carefully made as in dividing blood vessels, and the possibility of inducing elephantiasis should be considered.

The antecedent symptoms of chyluria are aching pains in the back and pelvis, but obstruction of the urinary flow (due to a chylous clot), may be the first indication, and there may simply be milky urine.

On standing, chylous urine coagulates and separates into three

strata, creamy on top; thick and milky and at times tinged with red, in the middle; and a sediment of reddish color at the bottom. The albumin reaction to heat is present and the lower layer contains red blood cells and lymphocytes and the ordinary urinary deposits. In the middle and upper layers fat is abundant, particularly in the upper, cream-like layer. Living filaria embryos are to be found, as a rule, in all of the layers. The condition of chyluria is not essentially fatal and may spontaneously disappear. Coagulation-plugging of the urethra may take place in the bladder, but is usually brief and non-fatal.

The drug **treatment** of the condition is unsatisfactory. Rest in bed, posture, (hips elevated) and a fat-free diet are indicated during acute attacks. If a simple chylous effusion of the tunica vaginalis be present, aseptic puncture and the injection of an irritant (as in the cure of hydrocele), to cause obliteration of the sac, may be performed; or the open operation, packing the sac with gauze, may be done to give relief from the inconvenient swelling.

The condition of true elephantiasis of the scrotum is far more amenable to surgical treatment than simple chylous varicose conditions. The *operation of removal* has a low mortality and is generally satisfactory. Essentially it consists in separating the hypertrophic tissues (skin and included mass of areolar tissue containing the testes and penis), from the sound, uninfiltrated tissues above, by careful dissection and forming from the stretched but sound integument above a new scrotum, if possible. The sheath of the penis must often be sacrificed and new coverings provided so far as possible. Otherwise it must heal by granulation; or skin grafting may be attempted. Preliminary hemostasis may be secured by elastic ligature of the mass. The incision lines consist of a transverse perineal line, a transverse line across the pubes anterially, and lateral lines, curved or straight according to sound tissue, connecting these two. Hemorrhage must be controlled as the operation proceeds and ligated vessels only should be trusted. The penis and testicles are released from the tumor by anterior perpendicular incisions. Important matters

requiring attention are the protection of all raw surfaces by some impervious non-adherent dressing material and a voluminous cushion-like outer dressing, for protection, firmly kept in place by a T bandage device from a circular bandage about the waist. Scrotal tumors have attained the weight of 200 lbs.

Large vulvar tumors (elephantiasis) may sometimes be treated by appropriate surgical operation, and breast tumors may also require removal. These tumors may vary from five to twenty-five pounds in weight.

Surgical procedures are less valuable in elephantiasis of the legs and arms. In elephantiasis of the legs a circumference of nearly three feet may be attained. Local skin elephantiasis (thickening) may be removed by operation.

The West African skin disease known as "Craw-craw," a papulo-pustular, itching eruption of uncertain pathology and symptomatology, and of doubtful specific identity, has been associated with filariosis by reason of the accidental discovery of filariæ (corresponding rather closely to filaria sanguinis hominis) in the tissues underlying the papules by two observers, O'Neil (Lancet, February 20, 1875) and Neilly, of Brest, France, some years later.

The evidence pointing to the condition of Craw-craw as an expression of filariosis is insufficient to be convincing.

At the Third Annual Meeting of the American Society of Tropical Medicine, March 21, 1906, Dr. Chas. Wardell Stiles of the United States Public Health and Marine Hospital Service, described a parasite which is regarded as belonging to the family of filaria which measures from thirty-two to fifty-two mm. in length. It resembles a parasite described as occurring in certain South American birds and Stiles regards it as a tropical or subtropical parasite, for which Georgia, in the United States, will probably form the northern geographic border. The specimen described was taken from the ulcerated leg of an individual in the state of Georgia and Stiles considers it impossible to reach definite conclusions regarding it until the adult stage is observed and studied. In the meantime he looks upon it as a surgical infection rather than a medical one.

Laboratory Detection. The recognition of filaria sanguinis hominis in the blood is not difficult, the organism being sufficiently large and motile to attract the attention of even the indifferently trained observer. The procedure of preparing a drop of blood does not differ from that in other blood searches. If the ordinary wet films be sealed by vaseline to prevent evaporation and drying, they can be made at night, during the peripheral activity of filaria nocturna, and examined later, the living filariæ remaining alive for several days, or even a week, providing the vaseline sealing be perfect. A low power objective enables one to discover the parasites and they can then be placed under the higher power glass.

To Stain the Parasite. Make blood smears from large drops of blood, spreading each to cover at least a square inch upon the glass slide. Dry in the air and stain either at once or at a later convenient time, the air dried films remaining serviceable for a long time. To stain the filariæ the hemoglobin should be dissolved out of the film, at least in part, and this may be effected by immersing the slide in water for about ten seconds, then drying and fixing with absolute alcohol. After this a weak, methylene blue solution or a weak carbol fuschin stain may be applied for twenty minutes or more; or a concentrated alcoholic solution of carbol fuschin, or a saturated aqueous solution of methylene blue may be used, applying the concentrated stain for a moment only, and washing thoroughly afterwards to remove the excess of the dye. Hematoxylin also stains the parasite well.

If it be desired to study the evolution of filariæ within the mosquito, several sections or dissected preparations of filaria-fed mosquitos may be made upon consecutive days, in which case the changes which I have briefly sketched may be studied. Culex fatigans mosquitos which have never been fed upon blood, and preferably those raised from the eggs, may be permitted to bite a person known to harbor f.s.h. nocturna, under a mosquito canopy at night, the hungry insects being set free within the net about midnight. In the morning the mosquitos, torpid and full of blood, will be clinging to the canopy and can be collected and

placed in a glass jar for future study, water and food (a slice of banana), being placed in the jar in which the insects are confined. The banana should be renewed daily. A mosquito can now be examined each day and the study of the evolution of the parasite within the insect may thus be followed. At least fifteen mosquitos should be permitted to feed upon the human host on the same occasion, should it be desired to study the complete evolution of the parasite in daily observations. The collapsed and empty sheath of the worm may also be observed in the mosquito's mid-gut after ecdysis occurs.

The student in regions where filarial infections are common may study the life of the filaria in the definitive host, in the dog, canine filariosis being extremely common in certain tropical countries, particularly in southern China. The canine parasite differs in size and in other respects from filaria sanguinis hominis but the evolution of the filaria is essentially the same as that of the parasite which infects man. The embryos may be studied in the peripheral blood of the dog, after which the animal may be killed and the adult filariæ may be found in the heart in pairs and bundles, males and females, the latter reaching a length of ten or twelve inches. This plan of study of canine filariosis was suggested by Manson in his lectures in San Francisco, in 1905.

CHAPTER III.

TRYPANOSOMIASIS.

Definition. Trypanosomiasis is a condition of animal parasitism, common to man and the lower animals, in which trypanosomes, peculiar microscopic animal organisms, infest the blood, and probably other tissues, either passively and without appreciable detriment to the host, or pathogenically, giving rise to conditions of disease.

A subject of very recent recognition and incompleted investigation offers great difficulties to the medical chronicler. If he narrates the current investigations and the incomplete observations and experiments in progress at the time of his writing, he will probably cumber his pages with theoretic material which may be disproved before the printer's ink is dry, and if he refrains from referring to unproved theories some important truth may be evolved, established and accepted in an equally short time, and his article, when it appears, will be incomplete and valueless. A middle course, therefore, seems to be the safest one. The accumulation of recent literature upon trypanosomes, in several languages, is very great and we can only undertake to consider the principal general facts concerning trypanosome infections, and will chiefly confine ourselves to human, pathogenic trypanosomiasis. Reference to all the works and medical journal articles consulted is impracticable, but a list of the most important sources of information will be found in the bibliography.

Flagellate animal parasites inhabiting the blood of fishes, amphibia and rats have been known for over half a century, and Gruby in 1843, described and designated such a flagellate, observed in a European frog, as Trypansoma sanguinis. Today a large number of species found in the blood of vertebrate animals, and in the intestines of both vertebrate and invertebrate animals, are recognized. Birds, reptiles, batrachians, fish, domestic animals, and man,

are the hosts of trypanosomes. The important varieties are, of course, those capable of producing disease in man and in the domestic animals, and the study of their transmission, morphology, reproduction and destruction is being actively pursued. The nomenclature of the great number of varieties of trypanosomes described is confusing, and the identity and relationship between the numerous similar parasites is too incompletely worked out to permit of classification as yet. The unscientific habit of designating these various organisms, by affixing Latinized proper names of the observers, contributes to the disorder. The following diseases of horses and cattle occur in Asia, Africa, South America, Southern Europe, Java, the Philippine Islands, and, rarely, in the United States, and have been definitely shown to be associated with, and due to, trypanosome infection. Tsetse disease, or Nagana, affects horses, dogs, sheep, and other domestic animals and is very fatal. It prevails in South Africa, is caused by t. Brucei and is carried by the biting Tsetse fly (Glossina Morsitans) and possibly by other insects also. Surra affects horses and water buffalo and is caused by t. Evansi. It prevails in India, Java and the Philippine Islands. Mal de caderas, caused by t. Equinum, is present in South America. Dourine, or Mal de Coit, is caused by t. equiperdum. Galzeikte, affecting cattle only, prevails in South Africa and is caused by a trypanosome twice the size of those already mentioned, t. Theileri. Many believe in the identity of Nagana or tsetse disease, surra and other horse and cattle diseases caused by trypanosomes.

Robert Koch (Deut. Med. Wochenschrift, 1904, 1705, XXX, No. 47), groups all trypanosomes into two groups differing in form, pathogenicity and virulence. In one group the morphology is constant, the trypanosomes are virulent for one single animal species and the virulence is constant. In the second group morphology, virulence and pathogenicity vary greatly. He believes that the parasites of the first group have lived for a long time in their respective hosts, and that the hosts have become immune to them, or tolerant of them. In this group are placed the rat trypanosome, found in thirty percent. of all rats, and the bovine

trypanosome of Thieiler, which causes a mortality of but five percent. Two parasites of Koch's second group may, it is believed, exist simultaneously in the same animal and can be made more or less virulent experimentally. Experimental infection of two different animals with the same trypanosome at the same time may produce severe symptoms in one case and trifling symptoms in the other. Koch reports success in immunizing animals against virulent trypanosomes by repeated injections of gradually increasing virulence.

McNeal and Novy, in the United States, first successfully cultivated trypanosomes outside of the animal body and have shown that individual animals (birds) free from trypanosomes so far as repeated blood examinations will show, prove to be infected when the blood is properly cultivated. The cultivation method of McNeal and Novy for certain varieties of trypanosomata included the use of ordinary nutrient agar into which defibrinated rabbit blood was introduced in varying amounts. Culture flasks sealed by rubber caps were used (Novy and McNeal). (Journal Infectious Diseases, 1904, Vol. 1, page 1.) This successful cultivation of blood parasites outside of the animal body is an achievement which has heretofore baffled investigators and has been looked upon as impossible.

It opens up a field for research of unmeasured possibilities. Of some interest as indicating the distribution of trypanosomes are the following observations (G. F. Petrie, The Practitioner, April, 1905). In five types of mammals examined for trypanosomes, thirty-three percent. of bats were positive; thirty percent. of the rats were positive; ten percent. of the wild rabbits were positive, and thirty percent. of the moles were positive. In the case of the field mole (meadow-mouse), all specimens examined proved negative. Sixteen and four-tenths percent. of the birds examined were positive for trypanosomes, six out of ten species containing parasites. Of fishes, nineteen gold fish were examined and all gave positive results.

Animal trypanosomiasis in Africa is so common as to be generally and popularly recognized as "fly disease," t. Brucei being certainly

carried by the tsetse fly, its intermediate host, whose bite to animals means disease and almost certain death. This fatal disease has killed off all the domestic mammals in certain fly-infested districts, and Bruce has shown that certain game animals (antelopes) are carriers of the trypanosome, while proof against its pathogenic properties; the parasites existing continuously in these game animals, and furnishing a permanent source of trypanosomes for tsetse flies which distribute them to domestic animals. Additional proof of this lies in the fact that with the disappearance of game, which follows occupation of the land by white men, tsetse fly disease disappears.

These observations all have a suggestive bearing, at least, upon the subject of human trypanosomiasis—a condition likewise extremely common and almost peculiar to the African continent.

Recently Dr. Fritz Schaudinn has announced beliefs, based upon investigations which he has made public, concerning the zoologic identity of certain protozoa, sporozoa, and flagellata which may, if accepted, make necessary the re-writing of much of the pathology and parasitology of several important tropic diseases. For example, he suggests the identity of spirochetæ and trypanosomes and the clinical identity of trypanosomiasis and relapsing fever. He also asserts that malaria parasites, at certain periods of their cycle, present trypanosome forms. If the dividing wall between animal parasitic diseases and those hitherto believed to be bacterial (as, for instance, relapsing fever) is thus broken down we may be approaching a re-classification of diseases which will either simplify, or render more complex, the study of tropical pathology at least. Upon the eve of such an important re-arrangement our attitude should be that of a tentative conservatism.

(Dr. Fritz Schaudinn, Arbeiten aus der Kais. Gesundheitsamte, 1904, Vol XX, page 387.)

HUMAN TRYPANOSOMIASIS.

So far as known at present, the only trypanosome affecting the human species is that known as trypanosoma Gambiense (also as t. Nepveui or t. Castellani), a flagellate blood parasite measuring

from 15 to 30 microns in length and from 1.5 to 2 microns in thickness. It may be described as an elongate flagellate and is a fusiform body provided with a fin-like undulatory membrane with a free border which is prolonged into a long flagellum at the anterior end of the parasite. At the opposite end of the body is a small spot, a centrosome, or micro-nucleus, while an oval nucleus appears centrally in the fusiform body. The body is often finely granular in appearance, although described as colorless and transparent. It is very motile, progressing with the flagellum end foremost, and is never intracorpuscular but remains free in the blood plasma. It is reproduced by longitudinal cell division, the original organism practically splitting into two. This form of division, ordinarily observed, is said to apply to the asexual phase of the organism, corresponding with the sporocyte (asexual) phase of the malaria parasite. It probably has a cycle of sexual development, which may take place outside of the blood.

Fig. 71.—Trypanosomes; showing ordinary structural appearance on left; in middle a trypanosome undergoing division; on the right an agglutinated group. (From Tyson's Practice.)

Medical interest in human trypanosomiasis rests, almost entirely, upon the identification of the condition clinically recognized as sleeping-sickness, as an advanced phase of human trypanosome infection.

SLEEPING-SICKNESS, known for at least a century as a prevalent and fatal disease occurring among the negroes of tropical West Africa, has within the past five years been almost certainly shown to be the result of trypanosome invasion giving rise to a meningo-encephalitis.

Facts of Geography and History. The distribution of sleeping-sickness, so far as known, extended until recently, from Senegambia to Benguela, West Africa, and the disease chiefly affected the tribes somewhat inland. During slavery days in America and the West Indies it was occasionally imported to the western

hemisphere in negroes sold into slavery but it never spread to individuals who were born outside of Africa, the necessary intermediate host and distributor of the disease, the tsetse fly, being lacking.

With the exploration and the commercial opening up of the African continent, the disease wandered from its original endemic area, extending along the Congo River and in other directions, so that today it is not only common throughout the Congo Free State but threatens Egypt as well, having invaded the Nile Valley within the past ten years. In portions of the interior of Africa, notably the Victoria Nyanza Lake region, it is epidemic to such an extent that the entire population of many villages has been destroyed and the country, in areas, is practically depopulated. While human trypanosomiasis has not been discovered in the American tropics, animal trypanosome disease prevails both in South America and in the Philippine Islands, and it is by no means impossible that the infection may be either introduced or discovered in some of our possessions—the necessary conditions for other fly diseases, and in fact the diseases themselves, as, for example Surra, being known to exist within our tropical domain. Occasional cases of sleeping sickness in imported negroes have, for years, been observed in London and Liverpool and the English government, naturally enough, on account of its Colonial and commercial interests in Africa, has sent medical commissioners to the scene to study the disease in all its phases. About the same time, the Portuguese Commission undertook a similar investigation. The British Commissioners were sent out in 1902, and their work has greatly cleared away the vagaries and removed the obscurity of sleeping-sickness, particularly as to its cause and manner of propagation. The two men who have done most to clear up these points are Castellani and Bruce and to them and their co-workers, some of whom made important suggestions, we owe the knowledge that t. Gambiense is found in the blood, cerebrospinal fluid and lymph glands in practically all cases of sleeping-sickness. The original discoverers of human trypanosomiasis were Nepveu, a French observer, about 1891, Forde, an English Colonial surgeon

in West Africa, in 1901, and Dutton, who recognized the nature of the infection in Forde's case and studied and named the trypanosome t. Gambiense. The patient in this investigation was an Englishman. Manson clinically studied a case of human trypanosomiasis in a white woman (a returned missionary) in England in 1902, and 1903, and Mott, studied the tissues post-mortem in the same case (1903), establishing the presence of the characteristic brain and tissue changes. The work of the commission included the determination of the fact that natives outside of the zones in which sleeping-sickness occurs are free from the parasite.

They also injected into the spinal canals or skulls of five monkeys the blood of a patient with febrile trypanosomiasis (not clinical sleeping-sickness) and while all five of the animals soon developed trypanosomes in their blood, one developed symptoms of sleeping-sickness, and upon autopsy the characteristic cerebral infiltration of sleeping-sickness was found.

Brumpt duplicated this experiment in another part of equatorial Africa, by twice inoculating a monkey, in the spinal canal, with the residue obtained by the centrifugation of 10 c.c. of cerebrospinal fluid, rich in trypanosomes. At the end of five weeks the monkey died of sleeping-sickness.

The English Commission arrived at the following conclusions:

Sleeping-sickness is caused by the penetration into the blood and cerebrospinal fluid of a certain trypanosome.

This trypanosome is probably t. Gambiense.

Febrile trypanosomiasis, as observed in West Africa is probably only an early phase of sleeping-sickness.

Monkeys are susceptible to the disease.

The trypanosome is transmitted by a tsetse fly, Glossina Palpalis—and by it only.

The distribution of sleeping-sickness is identical with that of Glossina Palpalis.

The work of Castellani in connection with these investigations is of a high order of excellence and completeness.

Etiology and Prophylaxis. Intimately associated with try-

panosome Gambiense, the cause of sleeping sickness, is Glossina Palpalis, the tsetse fly which conveys trypanosomiasis (and therefore sleeping-sickness), from the sick to the healthy. As classified at present, there are seven species of tsetse flies, all of them found in Africa, and of these at least two, Glossina Morsitans and Glossina Palpalis, carry trypanosome disease, the first to animals, the last to man. Glossina Palpalis is a common fly, inhabiting the wooded country and almost always found in the immediate vicinity of lakes and rivers. The larval stage of this fly is not, however, aquatic.

An unsettled question, as yet, is whether the fly acts as a true intermediate host or simply as a carrier of the parasite. The probability is that trypanosomes undergo an evolution of some kind, possibly a sexual one, within the tsetse fly. Analogy certainly suggests this, but the facts and details are not as yet satisfactorily worked out.

Other questions of interest in relation to the transmission of this disease are whether the trypanosomes are transmitted from fly to fly, either by hereditary transmission or otherwise, and whether other mammals passively harbor the trypanosome Gambiense in the same manner in which game animals harbor the trypanosome of Nagana (t. Brucei).

Prophylaxis. Knowing the cause and the distributor of human trypanosomiasis, the prevention is theoretically simple, namely, the banishment or destruction of the tsetse fly, *Glossina Palpalis*. Upon serious consideration, however, this undertaking will appear in its true magnitude, and the futility, at present at least, of attempting to control the threatening situation in Africa in this manner, will be apparent. Doubtless with a better understanding of the breeding and reproduction habits of tsetse flies will come measures whereby communities can destroy the flies and their breeding places locally and so limit the extension of the disease, but at present the preventive measures must be directed to individuals, both the infected and the healthy. The healthy individual should be protected from the bites of tsetse flies to prevent infection and the infected individual should be protected from the biting fly

in order that his disease be not spread to others. This protection should continue through both day and night. There is probably a limited infective period during which the fly can convey trypanosomes but this need not be considered in this connection. Tsetse flies should always be regarded as highly dangerous, and residents or travelers in tropical Africa should understand this fact and should always be familiar with their appearance. The best and most practical suggestions as to limiting the spread of sleeping-sickness are those which control the migrations of the natives and which subject them to isolation or detention in an infected district, upon discovery of the disease. Scientific diagnosis alone should be permitted to determine the banishment, detention or isolation of individuals. All of these suggestions can be enforced by Governmental authority and by such authority only, and the necessary details of quarantine should rest entirely with the Government officers.

Pathology. To the naked eye the pathologic changes are not striking and are practically confined to the central nervous system, the visceral changes being of uncertain character and causation. Splenic and hepatic swelling have usually been found postmortem, but these may have been secondary to concurrent diseases, as, for example, malaria. Evidences of active inflammatory processes in the brain are exceptional, although the meninges may present a milky appearance and a purulent meningitis may be present. Ordinarily, slight congestion and edema of the pia and arachnoid membranes will be observed. The purulent condition, when present, is believed to be due to a terminal infection and a streptococcus—(hypnococcus Castellani)—which was believed by members of the Portuguese Commission, and at first by Castellani also, to be the causative organism of sleeping-sickness, was observed in a good many cases. Usually, however, the principal pathologic evidences are microscopic. There is a constant small-celled monocellular infiltration extending over the entire cortex of the brain and into its substance, including the medulla and spinal cord, and when centrifugated many mononuclear cells are obtained from the cerebrospinal fluid. Mott demonstrated this infiltration

and found that it extended to all tissues of the body supplied with lymphatics. A similar condition was found to be present in monkeys, in whom the disease had been experimentally produced. Trypanosomes are found in the cerebrospinal fluid, and in the cervical lymphatic glands. They are also found in the pericardial, pleural and peritoneal fluids, when centrifugated.

Symptoms and Treatment. The clinical symptoms of human trypanosomiasis, as observed in the few instances in white persons in England, as already mentioned, seemed to be constant and distinctive. In at least one of these cases death occurred after the development of the symptoms of sleeping-sickness. The symptoms of trypanosome disease prior to the onset of the sleeping-sickness are as follows: Irregular and relapsing fever with intervals of normal temperature, the daily variation during the febrile attacks being from 1° to 2° F.; the gradual development of anemia or cachexia with the symptoms of dyspnea, palpitation and a rapid, feeble pulse; localized edema, especially about the eyes; enlarged lymph glands especially in the cervical region; progressive muscular weakness; enlarged spleen.

A peculiar eruptive manifestation of early trypanosomiasis is that of an ill-defined erythema, not clearly demarked, occurring irregularly over the body and limbs in circular patterns or in measly patches, the skin in these patches appearing slightly thickened or swollen. The blood shows a large mononuclear leucocytosis and t. Gambiense is present, either scantily or in considerable numbers, varying from one to eight to the film. That many of these symptoms pass unnoticed in the blacks in Africa is not surprising and there is no reason to believe that they do not precede the more conspicuous symptoms of sleeping-sickness.

The symptoms of sleeping-sickness in the negro may be described as those of a meningo-encephalitis. Headache, mental hebetude or torpor, or actual drowsiness are marked. The facial expression is dull and apathetic and while the memory is preserved cerebration is slow. The digestion is sluggish and the tongue is furred, constipation being the rule. Muscular spasms, epileptiform convulsions, tremor and paretic symptoms in general, gradually

develop. The superficial reflexes are preserved but the deeper ones are at first increased and then lost. The sensation is not greatly altered, except that a general hyperesthesia is usually present. Of the motor symptoms tremor is the most conspicuous, while late rigidity of the posterior muscles of the neck and contraction of the flexors of the knees and hips are usually present. The mental state is not usually that of paralytic dementia (which disease sleeping-sickness otherwise resembles), mania and the delirium of exaltation rarely being observed. On the contrary despondency and a consciousness of wretchedness is the rule. The disease usually runs a chronic course of from six to eight months, but it may be as brief as three months. Other symptoms, such as pruritus, muscular wasting, and prostration, with bed sores, may occur. The lymph gland enlargement, mentioned as an early symptom, persists and the spleen remains swollen. The victim may succumb to some intercurrent disease which his lowered vitality invites or he may die from exhaustion, or in a convulsion. The disease is positively fatal, so far as we are aware, no case of recovery having been recorded.

Treatment. In a disease invariably fatal, treatment suggestions mean little. Arsenic, quinine, and methylene blue have all been tried, pushed to the utmost limit of tolerance, and have been declared useless. Serum treatment has not yet been placed on a rational basis, injections thus far proving useless.

Although sleeping-sickness is doubtless an advanced and localized phase of trypanosome infection (a central nervous system infection), it is almost certain that all cases of trypanosomiasis do not terminate in sleeping-sickness. A few of the cases observed in whites are known to have existed for several years and it is a fact that in Uganda, a sleeping-sickness district in Africa, thirty percent. of the healthy natives harbor trypanosomes in their blood. Whether or not all of these natives will later develop sleeping-sickness we cannot say. The subject is one of too recent interest and study to permit of a definite statement in this matter. If the experiments of McNeal and Novy (loc. cit.) and of Koch, in immunizing animals, cultivating trypanosomes outside of the body

and attenuating their virulence, can be extended to t. Gambiense, there may be some grounds for looking forward to a rational and curative antitoxin or serum treatment, but at present the outlook is not particularly encouraging.

Shiga and Ehrlich have employed a synthetic product "trypanroth" with some success in the treatment of animal trypanosomiasis. The preparation is hypodermatically introduced and is followed, it is claimed, by a disappearance of the parasites from the general circulation, or by a decided reduction in their numbers, at least, at the end of forty-eight hours. Laveran and others view this treatment, in association with the internal use of arsenious acid, hopefully, in connection with human trypanosomiasis.

The preventive treatment, the all-important matter, has been discussed under prophylaxis.

Diagnosis. Neither febrile trypanosomiasis, nor sleeping-sickness, should be diagnosticated clinically, except perhaps in Africa in the districts where "fly disease" is endemic or epidemic. In cases of suspicious illness in travelers, returned from tropical Africa, especially intermittent fevers irresponsive to quinine, blood searches should be made, systematically and repeatedly, and the centrifuge should be made use of, examining the leucocytic layer in particular for trypanosomes. Specimens of cerebrospinal fluid may be obtained by lumbar puncture and treated in the same way, and puncture of the enlarged cervical glands may yield the trypanosomes. (See method described at the end of the Chapter.) The number of parasites found in the blood is not necessarily significant as to the severity of the infection, as they may be abundant upon one occasion and absent upon the next. Clinically febrile trypanosomiasis may resemble malarial disease or undulant fever, and sleeping-sickness may, as before mentioned. resemble paralytic dementia.

LABORATORY DETECTION OF THE PARASITE.

To discover the trypanosome in blood or cerebrospinal fluid use a $\frac{1}{5}$ or $\frac{1}{6}$ microscopic objective, a magnification of 300, plus, being sufficient. The oil immersion lens is unnecessary.

Fresh or stained specimens may be made use of. The Romanowsky method (see Malarial Staining) brings out the structure of the trypanosome. Films for staining are dried and fixed and then stained in a manner exactly similar to malaria parasite preparations. In moist films the parasites can readily be discerned (after some practice) moving about in the plasma. They are apt to impart a slight spinning motion to the red cells as they pass between them.

The appearance of the parasite has already been described. If the parasites are not abundant in the blood, puncture of a large lymph gland and examination of the lymph should be resorted to. The best method consists of puncture of the gland with the needle of a hypodermic syringe, the gland being squeezed and the piston of the syringe being withdrawn at the same time. In this way a few drops of lymph may be secured, and when blown upon a glass slide it may be subjected to staining and examination.

CHAPTER IV.

BILHARZIA DISEASE AND SCHISTOSOMUM JAPONICUM.

Synonyms. Bilharziosis, and Endemic Hematuria.

Definition. Bilharzia disease is a chronic parasitic disease of man, endemic in certain tropical countries and clinically characterized by hematuria, cystitis, and rectal irritation due to the deposition in the tissues of countless eggs of the causative worm, Schistosomum hematobium. The worm is also known as Distomum hematobium, and Bilharzia hematobia. Various complications and sequelæ accompany and follow this disease.

Facts of History and Geography. Various ancient historical writers indicate that bladder calculi were prevalent in Egypt, and Napoleon's soldiers, during their Egyptian campaign from 1799 to 1801, suffered extensively from hematuria. These were probably cases of Bilharziosis.

Dr. Bilharz, in 1851, discovered, while working in a hospital in Cairo, Egypt, that hematuria was usually due to the presence of schistosomum hematobium. The parasite was subsequently named in honor of its discoverer, Bilharzia hematobia. In 1864 Dr. John Harley found the worm in cases of hematuria observed in South Africa. In Cairo and in Lower Egypt Bilharz, Greisinger and Sonsoni found the parasites in from thirty-two to forty-two percent. of all postmortem cases, in one series of cases, and the occurrence of Bilharzia hematobia in a large percentage of the population of the lower classes of Egypt has long been admitted. Outside of Egypt and South Africa the disease, when observed, is usually of the imported variety, although occasional sporadic and apparently independent cases are observed in England and elsewhere in Europe. In Arabia, Syria, Persia and India the disease is not uncommon and in Mecca it is very prevalent. In Africa the parasite is found in Abyssinia, Soudan, Natal, in the interior, Tunis, Algeria, in the

Congo State, in the Sahara, in Angola and in the Zambesi basin. It has also been observed in Mauritius, Bombay and Shanghai, and in the West Indies, Porto Rico has been shown to present many cases, frequently in association with Ankylostoma infections. Recently the disease has been observed in California in the persons of Porto Ricans who had visited the Hawaiian Islands as laborers and then returned to America. During the past year several cases were observed in the United States in veterans of the Boer War.

Etiology and Prophylaxis. So far as observed the parasite affects males rather more frequently than females, but there seems to be no racial predisposition to the disease. In Egypt the condition is more prevalent in the early winter, and is frequently observed about three months after the annual inundation. It is believed to have an incubation period of from two to four months. Sandwith's article upon Bilharziosis in his "Medical Diseases of Egypt" and Manson's "Lane Lectures at San Francisco in 1905" contain very full and enlightening information concerning this parasitic infection.

The schistosumum hematobium is a two sexed trematode worm, milk-white in appearance, round and pointed at both ends and measures about one centimetre in length. Both of its ends are provided with suckers. The female is larger than the male. Its anterior half is white in color, the posterior half being gray, with brown longitudinal stripings which indicate the position of the intestinal canal filled with blood. When young the sexes live apart; when mature the female enters the gynecophoric groove or canal of the male which is formed by a lateral folding in of the worm. Within this canal the female remains, completely hidden at times. At other times, owing to its greater length, it protrudes from the gynecophoric groove or canal.

The portal vein is the principal habitat of the adult parasite but the young worms are also found in the liver, in the intestinal veins and in the bladder wall. The veins of the pelvis frequently contain the mature mated worms. In these various locations the worms are found mated and coupled, the male carrying the female with

him, embraced in the gynecophoric groove, as he penetrates the vessel walls in the submucous tissues of the rectum and bladder. The eggs of the female are laid within the veins, and by reason of their shape they penetrate the vessel walls to the tissues and there segment. They are yellowish in color, slightly transparent, and included within a thin shell. In shape they are fusiform with a central dilatation and at the posterior end is observed a spine from one to two-tenths of a millimetre in length. This spine is thorn-like and may appear laterally instead of terminally.

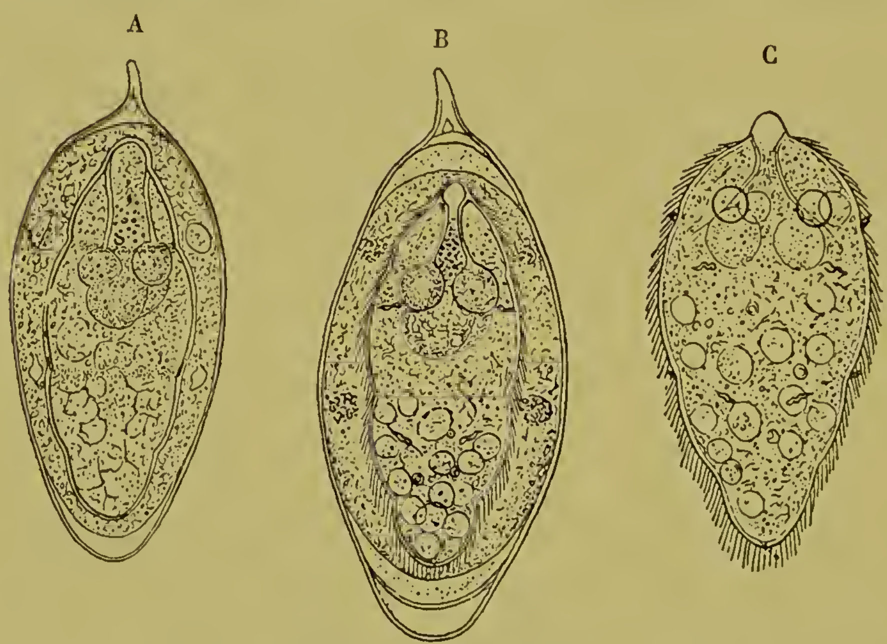


Fig. 72.—Ova and miracidium of *schistosomum hæmatobium*, × 300; A, ovum as seen in urine; B, the same after addition of water; C, miracidium. (Tyson after Railliet.)

The eggs may remain within the blood vessel and be carried by the blood stream into the liver. Upon reaching the capillaries the eggs may remain, held fast by pressure, or they may penetrate the vessel wall by the same force. In this way they give rise to local manifestations, and at length reach the cavities of the bladder and rectum, and escape in the urine or feces.

If the live egg is observed it will be found to contain a ripe miracidium which, under favorable conditions of warmth and water, escapes from the shell, actively swimming about in the water.

Specimens have been kept alive for thirty or forty hours but they usually die within a short time. (American Medicine, September, 1905.)

From analogy it is believed that the miracidium may enter the skin and reach the liver, in which organ only the very young worms are found. Here they probably mature, mate and join sexually, entering the large branches of the portal vein, travelling thence to the pelvic veins and organs. Here, as already described, they deposit their peculiar ova.

This hypothesis of transdermal miracidium-infection requires proof. The route by which the miracidium reaches the liver from its point of entrance in the skin, and the demonstration of its presence in mud and water, together with a lesion of the skin, must be established.

Claude Smith, of Atlanta, Ga., who reported seven cases of Bilharzia infection observed by him in the members of an itinerant show which visited the United States at the time of the World's fair in 1904, and which subsequently toured the country in 1905, relates his observations in "American Medicine" (October 14th, 1905), pages 656–659. Six of the seven persons observed to be harboring the Schistosomum Hematobium were ex-Boer soldiers and the other person was an African negro, all having become infected in South Africa. Smith examined urinary specimens from forty-one persons belonging to the traveling show and found that seven of these were infected. As there were at least 300 members of the aggregation, the parasites may have been generously distributed throughout the United States during their tour.

The urine of the seven infected persons (in all of whom the infection was chronic, and practically causing no inconvenience) presented no gross evidences of blood. Under the microscope red blood cells were seen and in two cases pus cells were present. Tube casts were not encountered but Bilharzia eggs, mature and immature, were plentiful. The immature eggs did not contain developed embryos, and were distinctly smaller than the mature eggs. In all of the eggs the spines were terminal, no lateral spines being observed. The embryo occupied the entire shell in some

cases, while in others there was room enough to permit it to turn completely around within the shell. The head was discernible through the shell, pointing towards either the sharp or the rounded end. A membrane lining the shell and enclosing the embryo was made out at the time the shell ruptured, and the embryo escaped.

The embryo was seen to be covered with cilia, with which it swims about. In the urine the egg shell does not rupture, and the embryos, therefore, are not free, and if the urine becomes decomposed, the eggs may die, retaining their shape and appearance, however. When the fresh urine is diluted, or when the ova-containing urine is passed into water, the shell promptly splits open and the embryo escapes. The larval parasite within the shell frequently changes its shape and position, and having escaped into water swims with great rapidity, having become somewhat elongated. A combined lateral rotation of the embryo has also been observed, both inside and outside of its shell. It has been suggested that the rupture of the egg shell and the escape of the miracidium is due to a lowering of the specific gravity containing the ovum, as, for example, when water is added to urine. This may not be the real cause, however, and it has been suggested that the embryo escapes through its own efforts, the violence of its movements rupturing the ova shell. Whether or not the escaped embryo now enters an intermediate host is not definitely known. Search for such a host has been unsuccessfully made among fresh water organisms, crustaceans, and larval insects. Loos suggests that possibly an intermediate host is unnecessary for the evolution of the parasite, and that the embryo directly enters the skin of man, as in the case of embryo ankylostomes. Experiments with monkeys to establish this theory have thus far been unsuccessful.

Concerning *Prophylaxis*, Sandwith (Medical Diseases of Egypt) says: "This most important section of all cannot be written until we know for certain how the parasite gains entrance to man; but I, for one, should now hesitate to bathe or paddle in water which might be infected, and for many other reasons it is unnecessary to lay stress on the importance of drinking only boiled or filtered water. In the meantime it is obvious that eggs which

have been passed in excreta should be rendered harmless by compelling patients to evacuate them into dry earth or sand, where the embryos cannot develop, and not in water."

Pathology. Pathological lesions due to Bilharzia parasites are found in the following organs, the urethra, bladder, kidneys, rectum, and liver. In the *urethra* these lesions consist of "small sandy patches" followed by fibrosis; stricture and fistulæ are also common. In the *bladder* the same sandy patches and the formation of fibrous tissue are observed, together with fissures, ulcers, hypertrophy and papillomatous or polypoid vascular growths. Calculi, having for their nuclei the ova of the parasite, occur in the bladder and also in the ureter. In the *kidneys* the secondary conditions of hydronephrosis or pyonephrosis are frequently observed. The organs may be cystic and present large dilated pelves. In the *rectum* the mucosa is distinctly thickened and granular but retains its vascular character. Ulcerations or polypoid growths may be observed, extending upwards to the colon. In the *liver*, which it apt to be greatly enlarged, a condition of cirrhosis is observed and white fibrous tissue is so increased that "its cut surface looks as if a number of white clay pipe-stems had been thrust through it at various angles." Whitish nodules of fibrous tissue also appear on the surface of the liver, and are found to contain the Bilharzia eggs. These nodular growths project from the capsule. The color of the parenchyma is usually drab. In the portal vein the worms may be found, either sparsely or in great numbers, a dram of blood sometimes containing as many as thirty parasites. The parasites may also be found in the inferior vena cava and the common iliac veins. The veins should be longitudinally incised to demonstrate them. On rare occasions Bilharzia eggs have also been found in the lungs, in the spleen, heart, pancreas, stomach and mesenteric glands.

Symptoms and Treatment. We find that the symptoms of Bilharziosis are such as might be expected from organs showing the pathologic changes just described. There is a general agreement between the severity of symptoms and the severity of the infection, or, in other words, the number of the parasites present.

If the infecting parasites are very numerous, symptoms are correspondingly grave, as a rule, although many cases of infection suffer no inconvenience whatever, at least for a number of years. This seems to be the case in the intestinal form of Bilharziosis especially. Manson (British Medical Journal, December 20, 1902) and Gunn (Journal American Medical Association, April 7, 1906) report such cases. It has been shown in many cases of the disease in Porto Ricans that the spines of the eggs of schistosomum hematobium found in the feces, in cases of rectal infection with the parasite, are placed laterally, and rarely if ever terminally. Some observers state that the lateral spined eggs also occur in the urine of Bilharzia cases occasionally, but so experienced an observer as Manson states that he has never seen a lateral spined ovum in urine. The suggestion that the lateral and terminal spined ova are from distinct species has been recently made but it is lacking in proof, at least, as yet.

A distinct and newly discovered human parasite closely resembling Bilharzia hematobia has been observed and described within the past three years. Special reference will be made elsewhere to this parasite, Schistosomum Japonicum.

The symptoms of Bilharzia disease are principally local, although anemia and resultant conditions are present when the loss of blood from hematuria is considerable. In certain studied cases a marked increase of eosinophiles was observed but it is impossible to state that this occurrence was due to the presence of Bilharzia parasites, complicating ankylostomiasis being present in most cases. In Egypt and in Porto Rico such concurrence of infections with the hook-worm and the Bilharzia parasite are very common.

After an incubation of from two to four months, vesical symptoms may appear. An early symptom is the appearance of a few drops of blood at the end of urination. This is caused by the rupture of a blood vessel filled with the sharp spined eggs, due to contraction of the bladder. Vesical and lumbar pains appear about this time, and an increased frequency of desire to urinate and a reflected pricking sensation, either in the prepuce or at the root of the penis, may be observed. Catarrhal cystitis now devel-

ops, and purulent or septic cystitis, due to the entrance of pyogenic organisms, may occur and may even prove fatal. The urethra and seminal vesicles may share in the inflammatory process, invariably due to the irritation of the sharp spined eggs. The hypertrophic, ulcerative and obstructive conditions described under pathology may now appear and interstitial nephritis may develop. Calculi form about the dead ova and give rise to symptoms according to their location, vesical, ureteral or renal. Perineal fistulæ or sinuses may occur and periurethral abscesses or stricture may result. Rectal inflammatory symptoms of varying degrees result from the presence of the eggs in the rectal tissues. A mucous discharge, tenesmus, and finally bloody discharges and actual prolapse of the rectum may occur, and an ulcerated condition with discharging sloughs may simulate dysentery. In the female, subacute vaginitis, as well as cystitis may be present. When death occurs it may be due to nephritis, exhaustion, septic cystitis or suppuration. Pain in many of the aggravated conditions described is unremitting and hastens the condition of exhaustion.

The mortality in Egypt (Sandwith) in 1684 hospital cases, many of them grave ones, was 5.8 percent. As fifty percent. of the lower class Egyptians are said to have endemic hematuria, and as the vast majority never appear at the hospitals, the true mortality is difficult of determination.

Medical Treatment with a view to curing the disease or destroying the parasites is useless. The relief of symptoms and the comfort of the patient (often impossible to secure) should be the goal of our efforts. The local effects of the Bilharzia eggs, especially the bladder effect, require treatment. If the symptom of pain is sufficiently urgent anodyne drugs or anodyne applications, warmth, etc., should be resorted to.

The antiseptic drugs usually prescribed in cystitis have a limited usefulness. The drugs used in bladder Bilharziosis include salol, sandal wood, copaiba, urotropin, or cystogen, and similar preparations.

Instrumentation and bladder irrigations are dangerous and

are to be resorted to only in cases of extreme catarrh or of purulent cystitis.

In the cases of rectal Bilharziosis, we may use soothing or medicated enemata and antiseptic local treatment.

Stone in the bladder, perineal fistulæ, stricture and similar surgical conditions, demand surgical treatment. Calculi in adults should be removed by lithotrity, if the urethra be patulous, and in boys by lithotomy. Sandwith mentions a series of 124 consecutive cases of lithotrity performed in Egypt without a death. Perineal section may be necessary at times, either for drainage of the bladder, or for the removal of a large bladder blood clot causing retention of urine.

The patient should avoid hard work, fatigue, alcohol, and a stimulating diet, and should lead a sane, temperate life, protecting himself from cold or other conditions liable to aggravate or excite inflammations of the bladder and urinary tract.

Diagnosis. The diagnosis of Bilharziosis is important and easy. It should be made by examining the urine and feces for the ova of Schistosumum Hematobium. The method will be described in the following section.

The possibility of concurrent infections has been mentioned and should be borne in mind.

The urinary specimen for examination should be the last portion voided from the bladder. If the entire specimen is supplied it should be centrifugated and the urine decanted, the precipitate then being examined microscopically.

LABORATORY DETECTION OF THE OVA OF BILHARZIA PARASITES.

Having secured the specimen of urine in the manner just described, prepare a cover-glass preparation of a drop of the suspected urine, and examine first under the low power objective and then under the $\frac{1}{6}$ objective. The characteristic cylindric, fusiform eggs, armed at one extremity, or perhaps upon one side, with the thorn like spines, will readily be seen. Under the higher power objective the structure of the egg and of the contained

embryo may be made out through the thin, transparent shell. If the drop of sediment obtained by centrifugation be diluted with water before the cover-glass is applied the phenomenon of the bursting of the shell and the escape of the miracidium may be seen. The cilia with which the embryo is covered are transparent, but they may be seen when viewed in profile. Before rupture of the ovum shell, it will be observed that a number of globules, lying beside the embryo itself, are included within the delicate membranous envelope. If the specimen to be examined be from the rectal discharges, a portion of the mucoid material should be selected and treated in the manner similar to that described for the urinary sediment.

These preparations need not be stained.

SCHISTOSOMUM JAPONICUM.

Synonym. Schistosoma Cattoi.

In 1904 Katzurada, in Japan, discovered a new parasite closely resembling the Bilharzia parasite and occurring in man and in cats. A few months later Catto discovered the same parasite in a Chinaman at Singapore, dead of cholera. Blanchard in Paris examined specimens of the worm and pronounced it a new species of Schistosomum. He bestowed upon it the name Schistosoma Cattoi, in honor of Dr. Catto.

Within two years considerable information concerning this trematode has been gathered and we now know that S. Japonicum (or S. Cattoi) is a bisexual trematode parasite of man, and of at least one domestic animal (the cat), and that it closely resembles the parasite of Bilharziosis.

It inhabits the blood vessels in man, probably the arterial side of the portal circulation in distinction from schistosomum hematobium which inhabits the venous side of the same system. Its eggs have been found in the intestine in association with those of ankylostomum duodenale and other common parasitic intestinal worms. It differs in size from Bilharzia hematobia in being smaller, the male worm averaging 10.5 mm. in length, and about 5.1 mm. in thickness; the female seems to be slightly longer and

thinner. The dermal coat of the male is smooth and the parasite is provided with two suckers. The eggs of the female, found in her uterus and in the intestine and in various tissues of the body in infected persons, differ distinctly in appearance and form from these of s. hematobium, being yellowish-brown in color, very thin shelled, and oval in shape. They are without spines, either lateral or terminal. The contained miracidium is ciliated and has been found free (escaped from its shell) in feces within the intestine. So far as known the parasite does not escape from the blood vessels, being chiefly found in the mesenteric arteries. The ova are too large to enter the capillaries, but in some manner penetrate the vessel walls and are found chiefly in the mucous and submucous coats of the intestines, both large and small, including the vermiform appendix. Upon section of these structures the eggs are found to be so numerous as to form a veritable layer in the intestine, which is thickened throughout, especially in the colon and rectum. They are also found in the liver which is hypertrophied and nodular and shows an increase of connective tissue. They are found in the mesenteric lymph glands (which may be enlarged to the size of walnuts) in the gall-bladder wall and the pancreas. These eggs resemble those of ankylostomum duodenale and Catto believes that this resemblance accounts for the fact that they have not been recognized heretofore. The bladder and urinary tract have thus far failed to reveal the ova and they are not believed to be present in the urine.

The symptoms associated with infection of Schistosomum Japonicum, and believed to be due to the invasion of the tissues by her eggs, are enlarged spleen and liver, enteritis, diarrhea with bloody stools, anemia, and exhaustion.

Infection with S. Japonicum is known to occur in the Islands of Japan and in China and it has recently been demonstrated in the Philippine Islands by Wooley (Philippine Journal of Science, January, 1906). A careful watch should be kept for it in the other American Tropics.

The life-history of the worm, as well as that of the embryo, is quite unknown as yet.

CHAPTER V.

ENDEMIC HEMOPTYSIS.

Synonyms. Distomum Pulmonale; Paragonimus Westermani; Distomum Ringeri; Fluke Worm of the Lung.

Definition. Endemic hemoptysis is a condition of blood spitting due to the presence in the lung of a fluke worm, variously designated, and belonging to the genus Paragonimus, an hemaphrodite trematode of undetermined life-history, which in its stage of human parasitism has its habitat in the lungs, where it surrounds itself by inflammatory exudate in small cystic tumors which communicate with the interior of the bronchial tubes. Through these openings the ova escape and are coughed up in the bronchial secretion, mixed with blood. The parasite itself is rarely coughed up, but the sputum in cases of endemic hemoptysis is loaded with brownish-yellow eggs with thin shells which average ninety-three microns in length by fifty-seven microns in breadth. The adult parasite resembles in size, shape and color a small watermelon seed. It averages nine mm. in length by five mm. in breadth and has two equal sized suckers, an oral sucker near the extremity and a ventral sucker which is placed about the middle of the body. Digestive and reproductive systems can be made out and the integument is covered with scale-like spines or spicules. The egg, magnified 500 times or more, is distinctive and when found in the sputum is diagnostic (see cuts). Our knowledge concerning the development of the egg outside of the body is limited to the fact that a ciliated miracidium develops in each egg after some weeks' exposure to water, escapes from the opercular opening in the shell and swims about in the water. Whether it now enters some intermediate fresh water host or not is purely speculative. In the human lung the cyst may contain either one or two parasites and their presence is not always productive of hemoptysis, though they may excite cough. There

may, however, be considerable breaking down of lung tissue about the cystic tumors, and fatal hemorrhage may even occur. This parasite also inhabits the lungs of animals, both wild and domestic, specimens having been encountered postmortem in tigers, and in dogs, cats, and pigs.

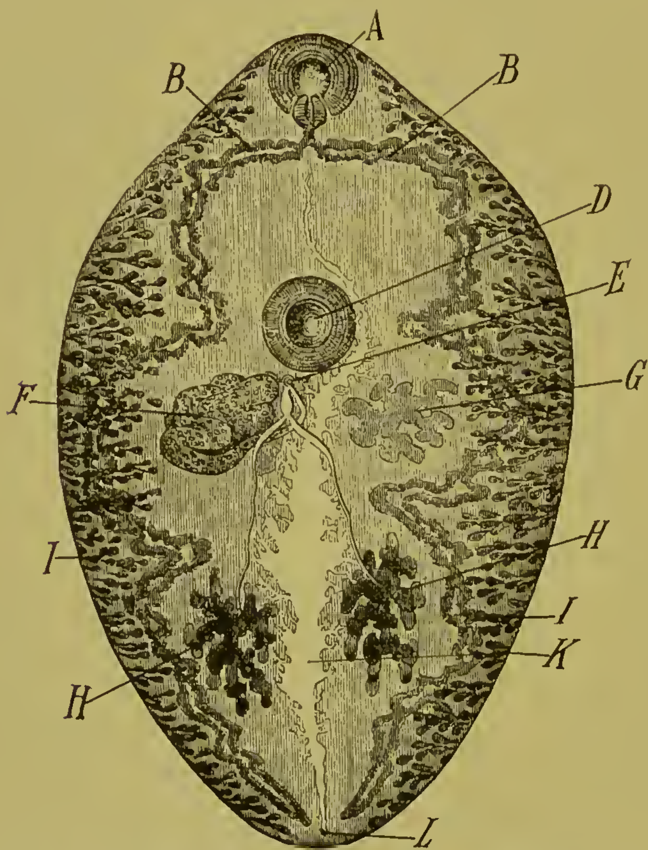


Fig. 73.—*Paragonimus westermani:* (Fluke worm of the lung.) (Ventral view.) 10 × 1. *A*, oral sucker; *B*, ceca; *D*, acetabulum; *E*, genital pore; *F*, uterus; *G*, ovary; *H*, testicles; *I*, vitelline glands; *K*, excretory canal; *L*, excretory pore. (Braun, after Leuckart.)

Facts of History and Geography. The geographic distribution of the lung fluke worm has not been definitely settled. It has been found in Japan, Corea, China, the Island of Formosa, and in other portions of the Orient and can reasonably be expected to make its appearance in the Philippine Islands. It has been found in North America, both in man and in animals, in natives and Orientals. More than a few cases have recently been discovered

in various parts of the United States and the fact that domestic animals harbor the parasite should cause us to look for its appearance, particularly among the Asiatics, Chinese and Japanese, who are present in large numbers in the United States, Central America, the Hawaiian Islands and especially in Manila.

The parasite was independently discovered by Kerbert in 1878 and later by Manson, Ringer, and Cobbold (in association), and by Bälz and Leuckart. It has since been principally encountered in Japan by Katsurada and in North America by Stiles and Ward.

Etiology and Prophylaxis. Adult males seem to be more frequently infected than other persons, but the method of infection is not definitely known.

Prophylactic measures are limited, therefore, to the disinfection or destruction of the sputum, containing the ova of the parasite, from known infected cases.

Pathology. Postmortem we find the characteristic cyst-like tumors, each filled with brown viscid fluid and traversed by burrows or canals, each leading to the interior of a bronchial tube or to another cyst. One or more parasites will be found in the tumor, which varies in size from that of a hazel-nut to a walnut.

Fig. 74.—*Paragonimus westermani:* (Fluke worm of the lung.) Photograph from a sexually immature specimen. (Tyson.)

From the discovery of soft, cystic neoplasms containing many eggs, in the brain, testes, liver, and elsewhere in the body, it has been supposed that the lung fluke sometimes enters the blood current and is thus carried to the tissues of the brain and other organs.

It seems quite as probable that the eggs themselves are thus carried in the blood current, but some doubt has been cast upon this view, as Kamamori believes them to be due to quite another

parasite, as the eggs observed did not present the opercular extremities of lung-fluke eggs. He also found them in a cirrhotic liver and in an adenoma of the rectum (Braun's Animal Parasites of Man, 1905, page 162).

Symptoms and Treatment. The symptoms of endemic hemoptysis are cough, rusty sputum, occasional hemorrhages from the lungs and anemia (dependent upon loss of blood, and either trifling or grave). Some cases may exist for years without particular discomfort and without symptoms other than a chronic cough with the occasional raising of rusty sputum.

Fig. 75.—*Paragonimus westermani:* Natural size; to left showing ventral surface; to right showing dorsal surface. (Braun, after Katsurada.)

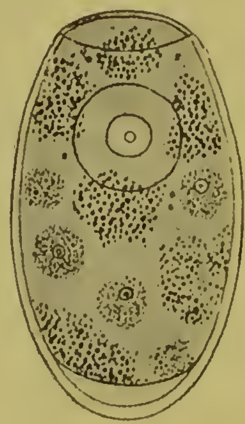


Fig. 76.—Ovum of *paragonimus westermani*, from sputum; 1000 × 1. (Braun, after Katsurada.)

Fig. 77.—Ovum of *paragonimus westermani*, from sputum. (Tyson).

Treatment by means of inhaled vapors, especially the vapors of balsams of various kinds, is alleged to be helpful and even curative in some cases.

Diagnosis. The symptoms may suggest pulmonary tuberculosis or pneumonia, but the physical signs of these diseases are absent, and there should be little difficulty in differentiation. Definite diagnosis rests upon the recognition of the ova in the sputum. Blood spitting should lead to a microscopic examination of the sputum for the ova of the lung fluke as well as for tubercule bacilli.

LABORATORY DETECTION OF LUNG-FLUKE OVA.

Make a smear of the expectorated sputum upon a glass slide, spreading with a platinum loop or simply dropping a cover-glass upon a drop of the sputum. Red blood cells will be found mixed with mucus and if the ova of the fluke worm be present they will be seen to be regularly oval in shape and brown in color, each provided with an operculum (a trap-door-like opening in the shell), at one extremity. This operculum furnishes the means of escape for the embryo from the shell. The eggs are extremely numerous and can scarcely be mistaken if observed. Staining is unnecessary.

CHAPTER VI.

GUINEA WORM DISEASE.

Synonyms. Dracontiasis; Dranunculosis; Medina Worm Disease.

Definition. Guinea worm disease is a condition of human infection with the guinea worm, or filaria Medinensis, a parasitic worm of the tropics, particularly common in Asia and Africa, which lives in the subcutaneous connective tissues of man. The worm is a long, slender nematode, occurring as male and female, and undergoing an intermediate existence in at least one other host, the fresh water cyclops. Its introduction into man is believed to be through the ingestion of water, or even of the intermediate host itself. The male worm has been discovered, according to C. H. Charles (Braun's Animal Parasites of Man), but its life-history is little known. It is believed to die after copulation, and to be smaller in size than the female worm.

Facts of Geography and History. The Guinea worm figures in history with some prominence, and Galen gave the disease its name Dracontiasis. The populous regions of Southwestern Asia, and Northeastern Africa, famous in both sacred and profane history, have harbored the parasite from remote times and the present distribution of the worm, while somewhat extended, is chiefly that of the centuries gone by. Guinea worm disease occurs in Arabia, Persia, Hindustan, and Africa, both coast and interior. In British Africa it sometimes affects the military forces to such an extent that ten percent. of a command may be ineffective from this cause alone. Both domestic animals and wild animals are known to harbor the Guinea worm also. It was imported into Brazil and the islands of South America but never became fastened upon these countries to any extent, except in the case of Brazil where the worm occupies a restricted area in some of the

river valleys. It is practically unknown in Europe and America although Osler mentions two cases, one in Philadelphia and one at Fort Monroe, which must have been contracted in the United States. In Eastern Asia and the Pacific Islands, it is not known to exist. It may be imported, however, into any tropic country, providing the necessary conditions, fresh water and the intermediate host, the cyclops, be present.

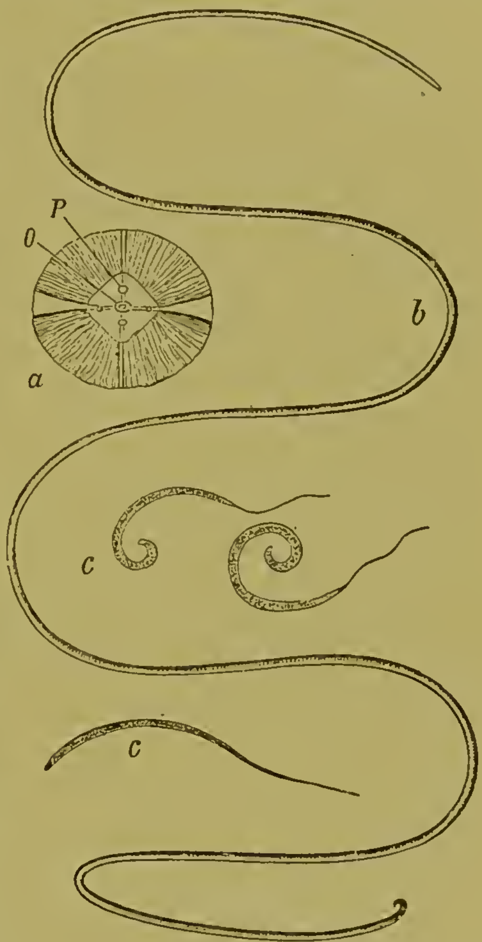


Fig. 78.—*Filaria medinensis: a*, anterior extremity; *O*, mouth; *P*, papillæ; *b*, female, reduced to less than half normal adult size; *c*, larvæ, enlarged. (Braun, after Claus.)

Etiology and Prophylaxis. The Guinea worm has an average length of about thirty inches, and an average thickness of one-tenth of an inch. Various observers have reported measurements of one-half to four metres in length and approximately a millimetre in thickness. This extreme dimension (4 metres) is open to some question. The worm is white in color, and in appearance resembles a violin string. The female worm is practically an elongated uterine sac, or tube, filled with a milky fluid which is literally loaded with young guinea worms or embryos. A digestive tube accompanies the uterine tube, lying beside it, and within a separate membranous envelope. Its anterior end is largest and there does not appear to be any anal orifice. One end of the worm is rounded into a head and provided with a small triangular mouth with six papillæ distributed about it; the other end terminates in a spine or hook of about 1 mm. in

length. Ovaries, vagina and vulva are supposed to exist, but cannot be made out in the mature female worm, the dilated, embryo-distended, uterine tube seemingly having caused their disappearance. The external or dermal coat of the worm is muscular. The embryo filariæ lie within the uterine tube in a coiled condition and are cylindric anteriorly but distinctly flattened towards the tails. In length they vary from 500 to 700 microns, and in thickness from 15 to 20 microns. The cuticle is transversely striated. The digestive tube in the embryo is relatively more distinct than in the adult female, and an anus and rudimentary genital organs can be made out. The embryos live in moist earth for six or eight days, and somewhat longer in water, especially if the latter be muddy.

Naturally, infection of man occurs through the embryo rather than through the adult worm. The principal views concerning the method of invasion are those of (a) ingestion of the larvæ in water; (b) the ingestion of an intermediate host containing the embryo worm, as, for example, the cyclops; (c) the penetration of the skin by the embryo after the manner of Ankylostoma larvæ, so brilliantly demonstrated by Loos, Claude Smith and others; (d) or the inoculation of the embryos by mosquitos, biting flies, or insects.

Any one of these hypotheses appears reasonable enough and the situation of the worm in man, in the subcutaneous connective tissues, seems to suggest the greater probability of a transdermal infection, but the whole question is as yet obscure.

Fedschenko, followed by Manson and Blanchard, has shown that embryo guinea worms, free in water, find their way into the interior of the fresh water cyclops, penetrating the integument of the cyclops, and developing within it until a length of 1 mm. (1000 microns) is attained. In the cases observed by Fedschenko this degree of development was attained in about a month. Moulting occurs several times during this period within the cyclops. The further development or fate of these embryos is not definitely known.

A rational *Prophylaxis* will include not only the avoidance

of unboiled water internally, in regions where the guinea worm is known to be endemic, but also the wearing of shoes while traveling through swamps, or stagnant water, as well as the avoidance of bathing in infected waters. The greater frequency of localization of the guinea worm in its human phase of existence, in the lower extremities of the body, suggests, somewhat strongly, that these members may be the original sites of penetration of the embryo worm.

Manson explains the appearance of guinea worms in the lower extremities (where they appear in nine cases out of ten), by the supposition that the parasite, by intuition or instinct, as it were, travels through the tissues of the human body toward the portion most frequently brought into contact with water, namely, the feet and legs. Certainly an hypothesis equally reasonable, and one which does not involve the exercise of instinct or intuition on the part of the worm is that of transdermal infection by the embryo worm, either by its own penetrating powers, as evidenced in its proven ability to enter the fresh water cyclops, or through the agency of the mosquito, as in the case of other filariæ.

Pathology. The lesions of guinea worm disease are rarely seen postmortem and so far as known they are confined to the subcutaneous and dermal tissues. If the adult female worm fails to penetrate the skin to the surface of the body, in her efforts to discharge her embryos, she may die and give rise to abscess formation. She may also fail to reach maturity, and, dying, may give rise to a hard cord-like swelling beneath the skin, which may persist for years. The lesions of the skin caused by the efforts of the worm in seeking the outer world are believed to be due to an irritating secretion discharged from the head of the worm. The first appearance of the skin lesion is that of a blister. When the blister ruptures, an area of ulceration, half an inch or more in diameter, is disclosed, in the centre of which is seen a tiny hole. Through this hole the worm sometimes protrudes its head, or the embryo worms contained in the milky fluid described, may be discharged through it. At times the uterine tube of the worm itself is projected through the openings for an inch or more, being

prolapsed through the mouth of the worm. The milky fluid poured forth will be found under the microscope to contain the embryos in countless numbers, curled up and motionless until brought into contact with water, when they take on great motility, swimming about freely, having evidently found a congenial element.

Symptoms and Treatment. The occurrence of Dranunculosis Medinensis in the lower extremities is often a serious matter, rendering locomotion difficult or impossible, and, according to the amount of ulceration and suppuration present, giving rise to febrile symptoms of some gravity. The infection may be either single or multiple, two or more worms frequently being found in the same individual, when commonly both limbs present the characteristic external lesions of guinea worm infection. The period required for the growth of the female worm to maturity is estimated at about one year and, as the worm approaches the surface to discharge her young, there may be systemic symptoms independent of the local ulceration and suppuration at the point of exit. These consist of temperature elevation and urticaria and are believed to be due to a toxin produced by the worm and absorbed by the human host. Pain, redness over the point of threatened skin puncture, and swelling resembling that of a phlebitis, corresponding with the position of the worm beneath the skin, may be present. The blister-like appearance and the superficial ulceration at the point at which the worm penetrates the skin have been described. After a penetration of the skin the worm may be induced, by the application of water in a small stream to the surface of the skin, to protrude her head and also to project the uterine tube nearly an inch at a time through her mouth, emptying it inch by inch of the contained milky fluid and embryos, until the entire uterine tube has been protruded and emptied, whereupon the remainder of the worm spontaneously expels itself or is removed. This "coaxing" plan of removal covers two weeks or more and is advocated by Manson in preference to the old-time practice of fixing the protruding end of the worm to a stick and daily winding upon it a portion of her

length. Frequently the worm, when so treated, breaks beneath the skin and the embryos escape into the tissues, causing inflammation, abscess formation and similar complications. The rapid method of extraction suggested by Emily, a French naval surgeon, and now successfully practised by a number of surgeons in India, Africa, and South America, consists of injecting within the uterine tube of the worm, by means of a hypodermic syringe introduced into the protruding head, one cubic centimetre of a 1 to 1000 solution of corrosive sublimate, which kills the worm and her embryos. Upon the following day, the dead worm may be easily extracted whole, resistance to traction disappearing with death. A modification of this method is the intracellular injection of the same solution, into or around the worm, when the head does not protrude. This likewise kills the worm, and incision over the verminous tumor permits of its extraction intact, or it may be permitted to remain, usually being absorbed without inflammatory reaction.

LABORATORY DETECTION OF EMBRYO GUINEA WORMS.

Place a drop of the milky fluid which exudes from the skin puncture in Dracontiasis under the microscope, using the lowest power objective. The embryo worms at once become visible in great numbers, each curled up in characteristic manner, its pointed tail extending outside of the circle formed by the body of the worm, but showing very slight motility.

If diluted with a drop of water each embryo becomes excessively active, retaining this activity for days.

For this examination a cupped slide or a watch crystal may be used and a two-thirds objective, or even a lower power lens, will suffice.

CHAPTER VII.

LIVER AND INTESTINAL FLUKE WORMS.

Fluke worms belong to the flat worms, and the order of trematodes and are generally small, leaf-shaped, or tongue-shaped and unsegmented. They are provided with one or more suckers; those supplied with a single sucker are known as monostomes and

Fig. 79.—*Distomum sinense:* To left a young example from cat (ventral view); to right a more mature specimen from man (dorsal view). (Tyson.)

Fig. 80.—Ovum and miracidium of *distomum sinense.* (Braun, after Leuckart.)

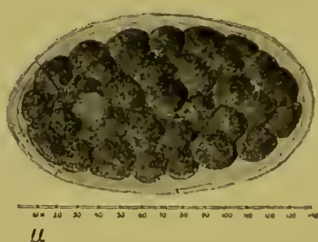


Fig. 81.—Ovum of *distomum hepaticum.* (Tyson.)

those with two suckers as distomes. They are hemaphroditic and self-fertilizing, although cross fertilization is also believed to occur. They are parasitic for mammals, fish, reptiles and birds and inhabit the cavities communicating with the surface by preference. The varieties for man are comparatively few.

LIVER PARASITES.

The following liver worms are occasionally encountered in man, although much more frequently in the lower animals. In some cases the parasites have been encountered in but few instances

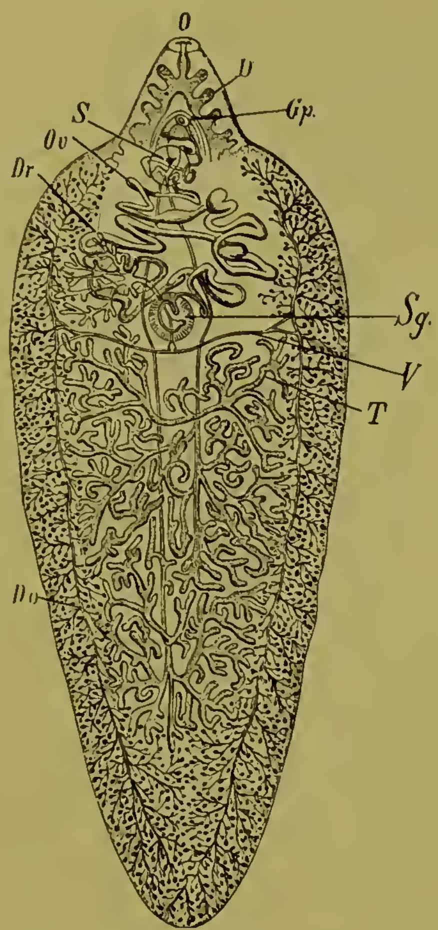


Fig 82.—Showing the sexual organs of *distomum hepaticum;* 5 x 1. *O*, oral sucker, *D*, intestinal ceca; *Do*, vitelline glands; *Dr*, ovary; *Ov*, uterine canal; *T*, testicles; *Sg*, "shell gland;" *V*, transverse vitelline duct; *Gp*, genital pore; *S*, ventral sucker. (Braun.)

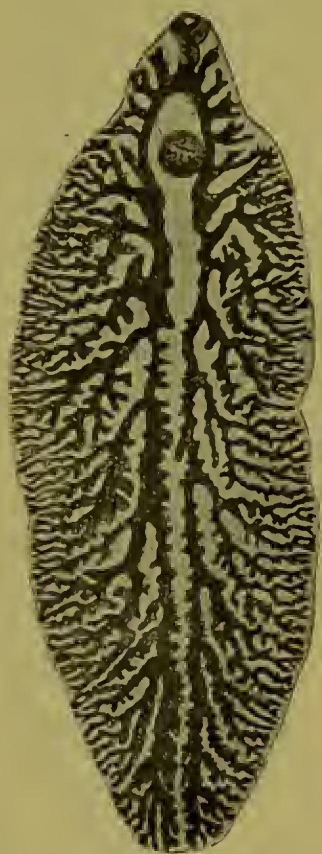


Fig. 83.—Showing the alimentary system of *distomum hepaticum*, other parts suppressed; 5 x 1. (From a fluke as yet undeveloped in its sexual organs.) (Braun.)

while in others they promise to prove rather important causes of disease in man. In a general way they are tropical in their occurrence. Most of them have several names. In this reference to liver flukes measurements and synonyms are generally omitted.

The interested student should consult some such text-book as Braun's "Animal Parasites of Man" for details.

Distomum Conjunctum is a fluke worm of slight importance. It has been encountered in man but a few times and is not believed to produce grave symptoms. It was found in the bile ducts.

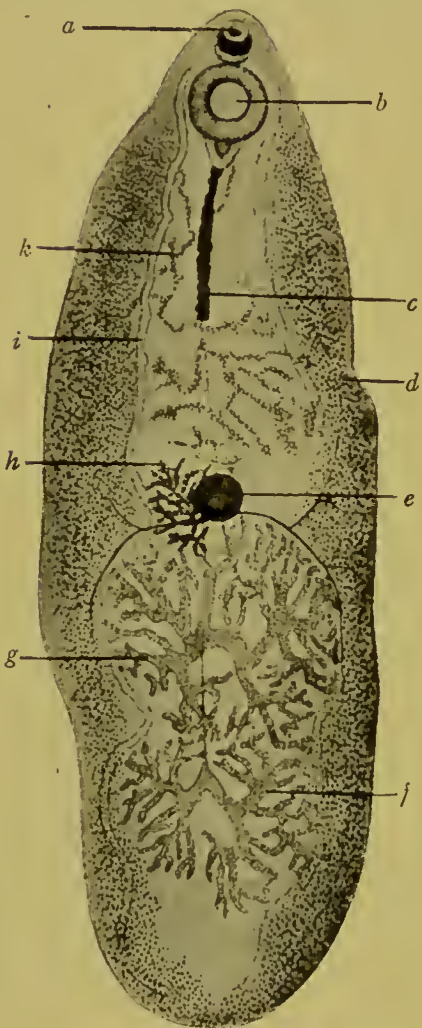


Fig. 84.—*Distomum buski: a*, oral sucker; *b*, acetabulum; *c*, cirrus pouch; *d*, vitelline glands; *e*, "shell gland;" *f* and *g*, posterior and anterior testicles; *h*, ovary; *i*, cecum; *k*, uterus. (Braun, after Odhner.)

Distomum Sinense is common in Japan, China and Eastern Asia, inhabiting the bile ducts as well as the intestine and pancreas. It resembles the lung fluke in its formation of cysts, except that the liver is the usual seat of the parasite, rather than the lungs. It causes hepatitis, enlargement of the liver, icterus, diarrhea and cachexia. Fourteen percent. of the hosts die from the infection.

Distomum Hepaticum is a large fluke worm infesting sheep, cattle, horses, and other domestic animals and occasionally met with in man. It sucks blood freely and in the sheep causes the condition known as "liver-rot," if present in sufficient numbers. In man its presence has only been discovered accidentally, at autopsy, no definite symptomatology being recognized.

Pentasomum Constrictum is an intestinal and liver parasite, not, however, of the fluke-worm variety. It has been observed in a number of cases in Africa by Aiken and Sandwith (in Egypt), the negro having been shown to harbor it. It occurs encysted in the liver and occasionally in the lungs, in its embryo form only.

It is multiple in occurrence, white in color, and measures from one to one and a half inches long. It is constricted or ringed and has a head armed with four hooklets. In the cases observed it was believed to be the cause of death.

INTESTINAL FLUKE WORMS.

Distomum buski and **Distomum rathouisi** are rare fluke worms inhabiting the upper intestine of man, a few instances having been observed in the Orient and in the United States. They are large flukes averaging 40 mm. long by 7 mm. broad, and are considered by Scheube and other observers to be identical. Their pathologic significance and their manner of transmission are unknown.

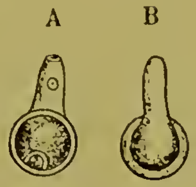


Fig. 85.—*Gastrodiscus hominis.* (Tyson.)

Gastrodiscus (Amphistomum) hominis is a rare fluke worm of the lower human bowel averaging 6 mm. in length and 3 mm. in breadth. It is of a red color and somewhat conical in shape. Its pathologic significance and life-history are quite unknown, but it is probably a parasite of the lower animals, occurring accidentally and but rarely in man.

CHAPTER VIII.

INTESTINAL CESTODES AND NEMATODES.

Intestinal worms are by no means limited to tropical regions. They are world-wide in their distribution and comparatively few are the varieties which are distinctly tropical. All come within one of the following families: Cestodes, Nematodes, and Trematodes.

Of the latter class, trematodes or fluke worms, we have discussed several varieties in the preceding pages.

Fig. 86. Bothriocephalus Mansoni. (Tyson.)

Of the Cestodes or tape worms, which, as is generally known, are flattened segmented worms, usually of great size, there are but four species which are essentially tropical. These are Tenia Nana, Tenia Madagascariensis, Tenia Africana and Bothriocephalus Mansoni. The first of these, Tenia Nana (Hymenolepis Murina) figures somewhat extensively in the Philippines. The second and third of these tropical tape worms occur in Africa, and the last has been observed in China, Japan, Australia and British Guinea.

Man is usually a definitive host for the tape worm, but in some cases the adult worms infesting the lower animals have their embryonic existence in the tissues of man, occurring there in a cystoidal form. This is true of T. Echinococcus which infests the intestine of dogs in its adult form and the tissues of man in its cystic form. It is probably true also for the last of the four tropical tape worms mentioned, Bothriocephalus Mansoni..

The general character of tape worms is too familiar and the worms are too universally distributed to require special discussion among tropical diseases. They are fully discussed in most medical

works. The important part of the tape worm is the scolex or head, from which arises a narrow neck which expands and becomes segmented. Each segment is a muscular sac containing the elements of reproduction and is motile and capable of discharging its eggs. The egg, escaped from the tape worm segment, in turn becomes the larval form of the worm. The intermediate host in feeding ingests the eggs and the embyro (cystic) stage of the tape worm develops within it. A few tape worms exist in their intermediate hosts without entering the cystic state, their larval form being that of a worm. In the cystic larval state the tape worm is taken by man with food, and within his intestines the scolex or head attaches itself to the mucous membrane, rapidly forming segments, the adult worm being thus reproduced and the life cycle completed.

It will thus be seen that each segment of a tape worm is endowed with the capability of reproduction. The tape worms are hemaphroditic and are without any tubular digestive organs, obtaining their sustenance in the human intestine by absorption. They vary in length from an inch or less to many feet, some specimens attaining a length of thirty feet. They also vary greatly as to the armament of their heads, some being provided with hooks, others with suckers, and some with both. The intermediate hosts are included in the zoologic range extending from fleas to cattle, and also to man, and a number of animals besides dogs act as definitive hosts.

The tropical cestode Tenia Nana, also known as t. ægyptica, has as an intermediate host the rat, and it also occurs in the rat in its adult form. Europe, Africa, North and South America and the Orient present this tape worm. It is less than an inch in length and its scolex is armed with a single circle of hooks. The number of segments is about 150. The ova are oval in shape and about thirty microns in diameter.

Concerning this worm the report of the Surgeon-General, United States Army, for 1904, states that in a battalion of the First United States Infantry, returned from three years' service in the Island of Samar, P. I., Tenia Nana was the intestinal

parasite of most interest, "being found in old chronic cases of bowel trouble associated with anemia. From one case about fifty specimens were obtained after a single dose of male fern, and from the other over a hundred. Owing to the difficulty of detecting them in the stools there is no doubt but that they were present by hundreds. Whether or not their removal will cure these old chronic cases remains to be seen." The clinical coincidence of infections with T. Nana and mental disturbance has

Fig. 87.—Tenia Nana x 10. (Gould.)

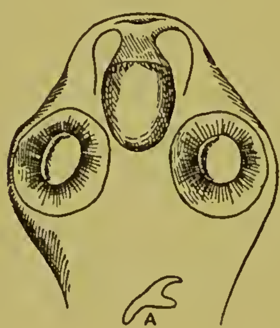


Fig. 88.—Head of Tenia Nana. (Gould.)

Fig. 89. Ovum of Tenia Nana. (Gould.)

been reported, but no definite conclusions or inferences have been drawn from the clinical facts.

The ordinary beef, pork, and fish tape worms, Tenia Saginata, Tenia Solium, and Dibothriocephalus latus respectively, need not be considered here. The latter variety is the largest cestode and may measure from fifteen to sixty feet in length. It is not a true tape worm, zoologically considered. (Gould and Pyle, Cyclopedia of Medicine.)

Of the **Nematode Intestinal Worms** or round worms, one of the most common in all climates is **Ascaris lumbricoides.**

It is reddish-brown in color, ten to twenty inches long and the head is armed with teeth. It occurs in both sexes and the female produces eggs by the million. These eggs have great vitality and withstand both heat and cold. The worm occurs singly or multiply, more than 100 frequently being encountered. The small intestine and the stomach are their principal habitat, but they sometimes migrate to the communicating cavities of the head, the bile ducts, etc. The eggs measure from sixty to seventy-five microns long and are about one-half as wide, being oval and bile stained and possessing roughened shells. The contents of the eggs are scarcely visible through the shell. The outer, rough, warty shell is often shed, however, and the egg may then resemble that of some other intestinal parasite, a point to be remembered in handling specimens for microscopic examination. Ascaris is not entitled to special consideration as a tropical parasite but it is extremely common and is often the unsuspected cause of gastric or intestinal irritation, and of vague dyspeptic symptoms, and, in children, of convulsions.

Fig. 90.—*Ascaris lumbricoides:* to left, male in lateral aspects; to right, female, ventral aspect, natural size. (Railliet.)

The Whip worm, **Trichocephalus Dispar,** occurs in the large intestine

almost exclusively and is from 35 to 50 mm. long, the female being slightly longer than the male. The females are much more numerous. This worm is common in the tropics, affecting a large proportion of the population, but it practically produces no symptoms. Its long, thin anterior portion resembles the lash of a whip, hence its name. Often it is found piercing a fold of intestinal mucosa like a pin with its sharp, thin, anterior portion. The eggs are distinctive and are present in great numbers. They are regularly oval except for the occurrence of a shining knob-like projection at each pole. These are, in reality, openings into the eggs, and are often plugged with mucus. The outer capsule is stained and thick and the inner one is thin and clear, showing the granular contents.

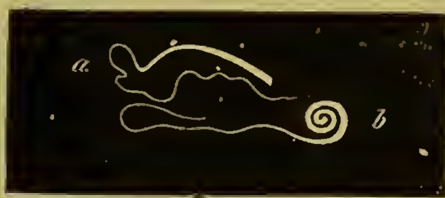


Fig. 91.—Trichocephalus Dispar. (Gould.)

The ordinary thread worm or seat worm, **Oxyuris Vermicularis,** resembles in appearance a piece of common white thread $\frac{1}{6}$ to $\frac{1}{2}$ inch in length. It has a pointed tail and a three-lipped mouth and inhabits the rectum and lower part of the large bowel in great numbers but it may find its way into the vagina. It produces itching and rectal irritation. The male worm is smaller than the female, the former measuring 3 to 5 mm. and the latter 9 to 12 mm. in length.

Rhabdonema intestinale or **Strongyloides intestinalis,** is a microscopic nematode worm 1 mm. long and fifty microns broad, inhabiting the mucus of the upper small intestine and known only in the female form. The eggs which are few in number may hatch in the intestines as well as outside of the body. Its pathologic significance is doubtful, and while it is believed to excite a catarrhal inflammation, it may be harmless. It is doubtless taken into

the human body in a filarial larval form, as the eggs hatch very promptly even within the human intestine. As it requires water for the development of this filariform stage it is probable that it is ingested by man in this medium.

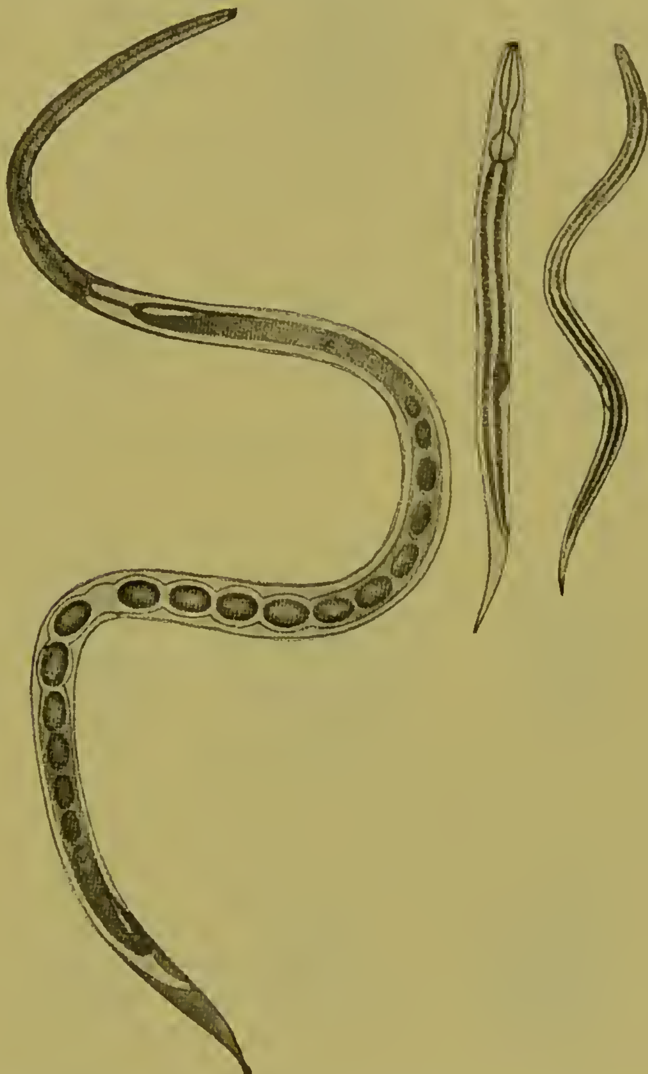


Fig. 92.—*Strongyloides intestinalis:* On the left a gravid female from human intestine (natural size, 2.5 mm). In the middle a rhabditiform larva from fresh fecal matter, × 120; to the right a filariform larva from culture, × 120. (Braun.)

The **treatment** of these various parasites may be considered briefly.

Round worms may generally be expelled by vermifuges, with

the exception of the whip worm which strongly resists expulsion. The most useful drug in the treatment of lumbricoid worms is

Fig. 93.—Eggs of parasitic worms. 1. Oxyuris vermicularis. 2. Ascaris lumbricoides. 3. Trichocephalus dispar. 4. Ankylostomum duodenale. 5. Tenia saginata. 6. Tenia solium. 7. Tenia nana. 8. Tenia flavopunctata. 9. Bothriocephalus latus. 10. Distomum hepaticum. 11. Distomum lanceolatum. 12. Schistosomum hematobium. (Cohen after Notter.)

santonin, and it may be advantageously combined with calomel. The dosage varies according to the age of the patient but it may

be safely exhibited in doses of from ½ grain to 3 grains. Exceptionally, yellow vision and a condition of intoxication is complained of, and the urine is apt to be stained yellow, but the drug is effective and reasonably safe. Santonin and calomel in combination may be given for three successive nights and should be followed in the morning by a saline purge.

Cestodes are generally best expelled by male fern. A dram each of chloroform and the fluid extract of male fern, in emulsion with an ounce of castor oil, may be given in the morning before food is taken. Food should also be withheld following the dose until the bowels are freely moved.

Of interest in connection with the subject of intestinal parasites in the Philippine Islands is the report of Captain Hallock, Assistant Surgeon, United States Army, which appeared in the Annual Report of the Surgeon-General for 1905. His observations were made at Ft. Porter, N. Y., and the report is quoted herewith:

"The command consisted of the Third Battalion of the First Infantry and returned to the States from the Philippines in May, 1903. While in the islands they were stationed at various points in the island of Samar.

"As many of the patients admitted to hospital for all causes were found to harbor parasites, I thought it would be of interest to examine the entire command, and the figures below show the result of this work and include only those who have served in the islands. Nearly all of the men were on duty and had no symptoms whatever. A few had slight disturbances of digestion and irregularity of the bowels, and some of the hook-worm cases had a little anemia, but not enough to give marked symptoms or incapacitate them for duty.

"No parasites were found in men who had not served outside of the United States. A number of the men were discharged by expiration of term of enlistment before the examinations were begun. In all cases reported as positive the ova or parasites were demonstrated at least three times on different days. These repeated examinations were made to avoid the possibility of error, for the

men were doing duty and brought their stools to the hospital, and occasionally the names were misplaced or lost. Cases reported as negative were examined on three days, and at least a dozen slides made in all.

	Company I.		Company K.		Company L.		Company M.	
	Number.	Percent.	Number.	Percent.	Number.	Percent.	Number.	Percent.
Men examined	54	....	30	....	30	....	40	....
Trichocephalus dispar	15	27.77	11	36.66	10	33.32	9	20.45
Uncinaria duodenalis	6	11.12	1	3.34	....	3.34	6	13.63
Tænia nana	1	1.85	....	....	....	....	....	....
Ascaris lumbricoides	1	1.85	....	....	....	....	1	2.28
Trichocephalus dispar and Uncinaria duodenalis	14	25.93	3	10.00	6	20.00	10	22.72
Trichocephalus dispar and Ascaris lumbricoides	1	1.85	....	....	1	3.34	....	....
Trichocephalus dispar, Uncinaria duodenalis, and Ascaris lumbricoides	1	1.85	1	3.34	....	....	....	....
Trichocephalus dispar and Tænia nana	1	1.85	....	....	....	....	....	....
Tænia nana and Uncinaria duodenalis	....	....	....	....	....	....	1	2.28
Negative	14	25.93	14	46.66	12	40.00	17	38.64
Number of men with parasites	40	74.07	16	53.34	18	60.00	27	61.36
Number of men without parasites	14	25.93	14	46.66	12	40.00	17	38.64

"Of the 158 men in the battalion 101, or 63.92 percent, harbored parasites.

"The following are the blood counts in three of the more marked cases:

	Case I—Diagnosis: Tænia nana.	Case II—Diagnosis: Uncinaria duodenalis.	Case III—Diagnosis: Trichocephalus dispar.
	Percent.	*Percent.*	*Percent.*
Polymorphonuclear neutrophiles	73.33	55.55	74.28
Lymphocytes, large and small	24.61	36.11	17.46
Eosinophiles	1.53	8.33	8.25

"I have been unable to form any definite opinion as to the source of the infections. One would naturally think of the drinking water, but the percentage of men infected in the different companies varies little, and they were stationed at many points in Samar and had many different sources of water supply.

"It is well known that the Chinamen who cultivate truck gardens in the Philippine Islands collect the night soil and after mixing it with water spread it on the grounds as a fertilizer. In connection with Loos' experiments with the *Ankylostoma duodenalis*, it is interesting to note that no history of ground itch could be obtained nor did the men go barefoot.

"The hook-worms were, as a rule, killed by thymol, but the effect was not satisfactory with less than six grams of the drug. This was habitually given in three doses of two grams each at intervals of two hours and followed by forty-five grams of Epsom salts or castor oil. The diet for twenty-four hours preceding the anthelmintic consisted of strained soup only, and a saline was given about three hours before the first dose of thymol. Occasionally it was necessary to repeat the treatment after an interval of a week or ten days.

"Male fern was efficient against the dwarf tape worm, but two of the cases which were apparently cured were found to have the parasites after two months, although they were present in smaller numbers.

"The round worms were all, as a rule, promptly expelled by santonin. One case, however, required 0.713 gram, and there was no toxic symptom from this dose. The drug was from a new supply and furnished by a reliable firm. In the preceding cases, with the old supply, 0.324 gram was always efficient.

"I have failed to dislodge the trichocephalus. The anthelmintics which were efficient against the other worms had no effect. Colon flushes of strong saline solution, quinine, and enemata containing turpentine were also without effect. The number of ova in these cases indicated but few worms, and I was unable to detect any symptom due to their presence."

PART III.

DISEASES OF UNDETERMINED OR UNCERTAIN CAUSATION (LOCAL AND CONSTITUTIONAL), AND SKIN DISEASES.

CHAPTER I.

ACUTE FEBRILE ICTERUS.

Synonyms. Weil's Disease; Infectious Jaundice; Icterus Infectiosus.

Definition. Acute febrile jaundice is a disease common in the tropics but not strictly limited thereto, characterized by a toxemic jaundice, fever, albuminuria, splenic swelling, pronounced nervous symptoms and a tendency to relapse.

Facts of History and Geography. The disease is common in Egypt and occurs sporadically throughout the world. It is not essentially a tropic disease, but, as a rule, occurs during hot weather. Having been encountered in the American tropics it will be described here. The condition can scarcely be said to have acquired the prominence due a distinctly accepted disease and it is omitted from many nosological tables. Many cases of typhoid fever with prominent hepatic symptoms, septicemic poisoning, and other conditions resembling acute febrile icterus have been mistaken for it but it is not unlikely that cases of febrile icterus are also overlooked, incorrect diagnoses of catarrhal jaundice, enteric fever, or even yellow fever being made. J. C. Wilson gives the following reasons for considering the condition a specific infectious process. (Page 808, Infectious Diseases, Modern Clinical Medicine, 1905.)

"The cases which correspond to Weil's description frequently occur sporadically but not rarely they appear in groups in circumscribed localities, and during the hot season. Males are more frequently affected than females—ninety percent. Certain occupations exert a predisposing influence, butchers, tanners and laborers in sewers being especially liable to the disease. It has been attributed to the drinking of contaminated water, and epidemics, especially among soldiers, have been ascribed to the swallow-

ing of such water during bathing. The disease is most frequent between the twenty-fifth and fortieth years of life. It is uncommon in childhood, and rare after fifty. The number of cases reported in America is limited. The researches of Jäger render it probable that an organism cultivated from the urine of living cases and from the organs of a case dead of the disease—*proteus fluorescens*—is the infecting agent. These observations have been confirmed by subsequent investigations."

In the Report of the Surgeon-General, United States Army, for 1905, Weil's disease appears upon the list of tropical diseases not thus far reported from the Philippine Islands.

Etiology and Prophylaxis. All consideration of the matters of etiology and prophylaxis would of necessity be speculative. We therefore omit them. Neither the manner nor the cause of transmission can be said to be definitely known.

Pathology. Postmortem the liver is increased in size and the spleen is swollen. The former organ may show cloudy swelling. The spleen is soft and distended with blood and the kidneys are swollen, acute parenchymatous nephritis being present in some cases. The liver is bile-stained but of larger size than the liver of acute yellow atrophy.

Symptoms. The onset of acute febrile jaundice is abrupt, being frequently introduced by a chill, and occurs usually without a prodromal period. The temperature rises rapidly to 104° Fahrenheit, or even higher, and the fever assumes a remittent type, lasting from a week to two weeks, relapsing, however, in a good many cases. Herpes of the face frequently accompanies the febrile period and occasionally an erythema is present. The digestive tract is more or less disturbed, as evidenced by a coated tongue, and frequently by diarrhea. Jaundice, either of a moderate or of an intense degree, appears upon the third or fourth day and if it be of a high grade, biliary coloring may disappear from the stools, leaving them gray in color. The nervous symptoms are well marked and the patient is apt to be stuporous. In severe cases delirium develops and coma always develops in the fatal cases.

Myalgic pains in the back and limbs set in early and remain late, and headache is pronounced. The muscles waste rapidly during acute febrile jaundice.

Hemorrhagic symptoms, such as epistaxis and hematuria, occur rather frequently, the urine containing red blood cells. Even if hematuria be not present, albumin and tube casts may be found in the urine. Intestinal hemorrhage and bloody sputum are also said to occur in some of the hemorrhagic cases.

In some cases tonsillar inflammation and more rarely parotid inflammation, followed by suppuration, have been reported as complications.

While the mortality of the disease is low, convalescence is tardy and the entire course of the disease, including the febrile period and convalescence, may extend over thirty days.

Treatment. The treatment is antipyretic and symptomatic. Purgation at the outset by a five-grain dose of calomel, followed by half an ounce of magnesium sulphate is advisable.

A suitable liquid diet and large potations of water are indicated. If the fever remains above 103° Fahrenheit, cold sponging or bathing may be resorted to and this treatment should be given preference over the administration of antipyretic drugs. Salol, or the salicylates, for their antifermentative effect, and for the relief of myalgic pains, may be used. Otherwise, the treatment should be determined by the predominance of the symptoms.

Diagnosis. Acute febrile jaundice bears a resemblance to all of the following diseases, enteric fever, malarial fever, yellow fever, and dengue. The clinical similarity to enteric fever must be apparent from the description given, but febrile jaundice may be differentiated from enteric fever by its sudden onset, the prominence of the icteric condition, the briefer duration and the absence of rose spots and the Widal reaction.

The absence of malaria parasites in the blood will distinguish it from malarial fever.

In the tropics the two diseases most likely to be confused with acute febrile jaundice are yellow fever and dengue. From the former we may distinguish febrile icterus by the temperature

curve, the absence of the characteristic pulse and temperature relationship of yellow fever, and by the absence of the pernicious gastric symptoms of yellow fever. Both diseases are accompanied by albuminuria, are of sudden onset, and are accompanied by jaundice.

The absence of albuminuria in dengue, the duration and general course of the disease, the initial erythema and, more especially, the polyform terminal eruption of dengue will serve to exclude this disease. Occasionally, as noted, a febrile erythema occurs in infectious jaundice, and both diseases are accompanied by myalgic pains.

I am informed, however, by a gentleman familiar with both dengue and febrile jaundice, that the differential diagnosis is often difficult during the early stages of dengue. The pronounced epidemic character of dengue, however, is a distinguishing feature.

The predisponents of age, sex and occupation, mentioned as peculiar to acute febrile jaundice, should be borne in mind in making a diagnosis.

CHAPTER II.

FEBRILE TROPICAL SPLENOMEGALY.

Synonyms. Kala Azar (Black Fever); Dum Dum Fever.

Definition. Febrile tropical splenomegaly is a specific parasitic disease due to infection with Leishman bodies and characterized by great splenic enlargement, irregular pyrexia, anemia, emaciation, dysenteric symptoms, ulcerations of the mucosa, such as noma vulvæ and cancrum oris, and sometimes by ulcerations upon the knees, elbows or legs.

By reason of its almost certain relationship to trypanosomiasis, this disease, definitely classified less than three years ago, should be considered in connection with trypanosome infections. It has been clinically known in India under various names, such as Dum Dum fever and Kala Azar, for some years and in Assam an epidemic, marked by gradual extension and a high mortality, began twenty years ago and the disease has slowly spread over the State, dying out and appearing here and there, in small epidemics, and even in isolated cases.

History and Geography. The disease probably has a wide tropical distribution, and is known to exist in China, Assam, India, Africa and Egypt. Thus far tropical America has presented cases in Panama and the Philippines and the disease will probably be discovered elsewhere, or imported along the routes of commerce. (See monthly Reports of the Chief Sanitary Officer, Panama Canal Commission, and the New York Medical Record, page 628, April 21, 1906.)

It will be unnecessary to review the history of this disease prior to 1900, during which year Leishman, a Major in the British Army Service, discovered the presence of the parasitic bodies, which now bear his name, in the spleen of a soldier returned as an invalid from India, who died in the Netley (England) Military

Hospital. Not until 1903, however, did he publish this report, following his discovery, in the spleen of a trypanosome-infected rat, of bodies similar to those observed postmortem in the soldier at Netley in 1900. Cunningham, in 1885, was probably the first to encounter these bodies and to regard them as parasitic.

Prior to this time various commissions sent out from India to study Dum Dum fever, or Kala Azar, had submitted a number of incorrect theories in regard to the causation of the disease but their findings were so dissimilar and incorrect that they need not be mentioned. Marchand and Ledingham (of Leipsic) found the parasites in the spleen, bone marrow and liver of a German soldier who took part in the China Expedition in 1900, and who died of febrile splenomegaly in Germany.

Donovan seconded Leishman's discovery and the parasitic bodies are frequently spoken of as Leishman-Donovan bodies. Laveran, Christophers, Rogers, Manson, Low, and others have contributed to the growing fund of information concerning these bodies, not, however, without exciting a controversy as to the proper classification of the newly discovered parasites. Some of the observers, Laveran in particular, classed them as belonging to the piroplasma; others grouped them with the trypanosoma and still others with the microsporidia. Manson and Low strongly insist that the bodies are not parasites of the red blood corpuscles.

It has been definitely established, at least, that these bodies, whether obtained from splenic puncture during life, or from the ulcerations which occur in febrile splenomegaly, undergo multiplication by division, and that in cultures outside of the body flagellate forms resembling trypanosomes develop after a few days' incubation at 20° Centigrade.

Etiology and Prophylaxis. The Leishman body, now generally admitted to be the cause of tropical splenomegaly, is demonstrable either stained or unstained; better, however, when stained by the Romanowsky method. The technique will be found in the last section of this discussion. The bodies are remarkably uniform in size and are round or oval in shape, and measure about 2.5 microns in diameter. They are sharply outlined when stained

and they seem to possess a cuticle, or a limiting membrane. Each body presents two striking, deeply staining, chromatin masses, one decidedly larger than the other, placed opposite each other in the shorter diameter of the body. Of these two chromatin masses the larger one is usually oval and stains less deeply than its fellow, which is generally rod-shaped. While the effect of the presence of these bodies upon the spleen is not entirely clear as yet, it is apparent that the enormous profusion of the parasites in the spleen, actually displacing and occupying the space of normal tissue elements, as shown postmortem, is sufficient cause for the fatality which attends tropical splenomegaly. The disease is now considered as necessarily fatal.

We are entirely without knowledge calculated to throw light upon proper prophylaxis in this disease and must await further developments in the life-history or evolution of the Leishman bodies, or their definite identification with trypanosomes. The determination of the zoological status of the Leishman parasite, and the means by which it passes from one human body to another, are interesting questions which await solution. Upon the latter question the experiments of Rogers, verified by Christophers, seem to throw at least a suggestion. It was found that the parasites multiplied by division and also developed into flagellate bodies under certain conditions outside of the human body. One of these conditions, as has been mentioned, was a constant temperature of 22° Centigrade, considerably lower than the human body heat, and this suggests (to Manson) an extracorporeal existence in a cold medium, possibly soil, water, or the body of a cold-blooded animal.

The occurrence of Leishman bodies in the ulcerating lesions of tropical splenomegaly also suggests to him that the parasites leave the human host by these exits. Doubtless these hypotheses will lead to further experimentations which may clear up the questions and point to rational prophylactic indications.

Pathology. The organ most conspicuously affected in tropical splenomegaly, is the *spleen*. In life, by splenic puncture, the Leishman bodies have been demonstrated in films or smears,

but postmortem their real relations are shown by microscopic sections and they are found to lie within cells of various shape, as follows (Stephens and Christophers):

a. Slightly modified endothelial cells;

b. Large, round cells each with a large nucleus;

c. Very large cells with two vesicular nuclei (very abundant in the liver and spleen);

d. Large, centrally vacuolated cells showing signs of necrosis.

In the first variety each cell may contain from six to twelve parasites; in the second variety twenty or more; in the third variety they are very numerous and in the fourth variety each cell is crowded with parasites to the point of rupture, the number sometimes reaching 250.

The gross appearance of the spleen is peculiar to tropical splenomegaly, the organ, greatly enlarged, is firm and friable but not fibroid in texture. It does not collapse upon removal from the body.

In the *liver*, also, the parasites are found, postmortem, to be included in cells of doubtful character. The parasites are characteristic, but the containing-cells seem to be within the capillaries and resemble macrophages. In gross, the liver appears firm and friable and does not collapse when removed from the body. On section the centres of the lobules appear to contain a white deposit (masses of the parasite-containing cells just described).

The *colon* is the seat of multiple ulcerations in a granulating condition. These granulations contain many parasites which are also included within cells. The same is true of granulating lesions elsewhere in the body.

In the *bone marrow* Leishman bodies, included in cells (macrophages?) are innumerable. They also occur scantily in mononuclear and polynuclear leucocytes and in myelocytes. In lymph glands adjacent to ulcerating lesions the Leishman bodies are also found, cell-included.

In the peripheral blood Leishman bodies are rarely found and are present only in the case of high fever, 103° or 104° Fahrenheit,

and then only within leucocytes. The red cells and hemoglobin in tropical splenomegaly show the changes of secondary anemia, the red cells usually being reduced to 3,500,000 to the c.mm. It should be borne in mind that malarial infection and hook-worm disease are frequently concurrent infections, to which the evidences of secondary anemia may in part be due. Poikilocytes and a few normoblasts may be observed. The leucocytes are generally reduced and leukopenia may be marked. In the presence of concurrent hook-worm infection the eosinophiles are apt to be increased. The blood-platelets are also increased.

Symptoms and Treatment. The symptoms of febrile splenomegaly, while apt to be mistaken for those of chronic malarial cachexia, a condition which may very possibly be present as a complicating factor, are apparently quite well marked.

The most prominent objective symptoms are those of splenic and hepatic swelling. These are gradual in their onset and the splenomegaly may be very great, the area of splenic dulness extending to the umbilicus, or even down to the pubis. The liver enlargement is generally much less marked. The fever, always present, may vary greatly as to type in different cases. It is usually irregular but it may be regularly quotidian or irregularly intermittent and it may change in type during the course of the case, and there may also be intervals of apyrexia lasting for several weeks. Usually there is a paroxysmal manifestation, an afternoon exacerbation preceded by a chill and followed by a profuse sweat, and this may easily be mistaken for a malarial expression, especially if a concurrent paludism, shown by the presence of malaria parasites in the blood, exists. Quinine, however, has no influence upon the fever of tropical splenomegaly. The fever usually persists throughout the entire course of the disease and may range from 101° to 104° Fahrenheit. Intestinal symptoms make their appearance in most cases when the disease is fairly well advanced and the stools become bloody and contain much mucus, but do not contain amebas unless an intercurrent amebic dysentery be present. The granulating intestinal lesions observed postmortem do not resemble the ulcerations of amebic

dysentery. Clinically, however, the cases are dysenteric, and surgical complications, such as perforation of the bowel, may occur, causing death. Ulcers of the mucosa, often serpiginous, appear in the mouth and upon the vulva, and the integument may also show papules, especially about the scrotum, or small granulating ulcers may appear about the knees, elbows and legs. In Madras, Christophers found that all individuals with cancrum oris, subjected to splenic puncture, contained Leishman bodies.

As secondary anemia advances, nasal hemorrhages, purpura, edema of the legs (inconstant) and dyspnea appear. The complexion is sallow or muddy. Sooner or later the patient, with protruding abdomen but greatly wasted limbs and body, takes to his bed and dies of exhaustion unless sooner destroyed by an intercurrent disease. The duration of the disease is variable, lasting either months or years.

Treatment. There is no treatment which in any way checks or modifies the course of the disease.

Diagnosis. There is but cold comfort for the victim of tropic splenomegaly in the knowledge that his malady is one that can be scientifically and accurately diagnosticated, and yet it is of the highest importance that his physician apply this scientific and accurate method of diagnosis. As already indicated, the characteristic Leishman bodies may be obtained during life by a splenic puncture and diseases which resemble tropic splenomegaly may be discovered or excluded by methodic blood examinations. The objective symptoms which would suggest the disease have already been set forth, and diagnosis in so vital a disease as tropic splenomegaly should never be made from objective symptoms alone, as a more decisive method exists. In this disease diagnosis should only be made upon the positive recognition in the spleen or other tissues of the Leishman bodies.

Tropical residence in a district where febrile splenomegaly exists, in combination with the symptoms related, constitute a basis for suspicion. We may exclude malarial disease by the therapeutic test of quinine administration and by blood examinations for the hemameba malariæ. Undulant fever may be excluded

by the serum agglutination test for micrococcus melitensis. This reaction does not occur with the serum of patients with tropical febrile splenomegaly if reliable cultures and reasonably high dilutions are used. The chief clinical resemblance is in the temperature range.

Leukemia (leukocythemia) should be suspected and the possibility should be investigated, as its presence contraindicates splenic puncture for material in which to search for the Leishman bodies. The wounding of a leukemic spleen might give rise to fatal concealed hemorrhage. The great increase of leucocytes in leukemia and their decrease in tropic splenomegaly, and the more profound alteration of the red cells, as to number, size, shape and condition of degeneration, in leukemia, will serve to distinguish between the two conditions. If the blood examination excludes leukemia and other symptoms warrant the suspicion of tropic splenomegaly, puncture of the spleen or liver with a sterile hypodermic needle may be performed. The desired object is to secure a particle of the splenic or hepatic pulp, and not the abstraction of blood. The method is given in the following section. It should be borne in mind that malarial disease, the most common of all tropic systemic infections, is frequently present in the subjects of febrile splenomegaly, and this complication may confuse the diagnostician.

LABORATORY DIAGNOSIS.

To perform splenic or hepatic puncture, use either a small aspirating needle, or better, a large hypodermic syringe. Naturally, the instrument must be made absolutely sterile by boiling, and therefore, a specially designed syringe should be used. Make the puncture between the ribs over the spleen or liver if the swelling is not sufficiently great to insure certain puncture of the desired organ elsewhere. If the enlarged organs, spleen and liver, appear distinctly outside of the thorax, choose a prominent point, being careful to fix the skin firmly over the tumor. Do not introduce the needle very deeply, and after

introduction slowly withdraw the piston. If no blood appears in the barrel of the syringe it is of no consequence, providing a minute sample of the pulp or juice of the organ be present in the needle, as will usually happen. The blood, let it be remembered, is not desired for examination. Pressure by strapping or bandaging should be made over the puncture site and the patient should remain recumbent after the operation. If the breath be held, with the lung deflated, during the operation, laceration of the capsule by the needle point and possibly bleeding, will be less likely to occur on account of limiting the excursions, with the diaphragm, of the spleen and liver.

Deaths have been reported as following this procedure and, consequently, the operation should be carefully performed and only in case of necessity. A single puncture should suffice. Liver puncture is probably less dangerous than splenic puncture. Having secured the specimen, even if but a drop or a small particle, it should be blown upon a glass slide, spread into films upon cover-glasses in the usual manner, dried, fixed and stained. If a fragment of granulation tissue be used, it should be placed between two glass slides and spread by pressure into smears, then dried, fixed and stained. Granulation-tissue fragments may also be imbedded and cut into sections. Fixing should be done with alcohol. Stain by the Romanowsky method (see malarial staining) or preferably with Leishman's stain (see formula elsewhere in this book). The appearance of the stained Leishman bodies has already been given under Etiology. The parasites may also be demonstrated, as before mentioned, in the bone marrow, the intestinal ulcerations and the granulomatous skin ulcerations.

CHAPTER III.

TICK FEVER.

The subject of tick fever is enshrouded with much uncertainty, but there is, and has been for years, a well-grounded belief among tropical clinicians and observers, that a definite relationship exists between the bites of certain blood-sucking animal parasites known as ticks, and attacks of paroxysmal fever in man.

In Africa diseases are known to be spread among mammals by several ticks, each, as a rule, conveying fever to some particular species. Sheep ticks, cattle ticks and dog ticks are known to be capable of disease conveyance and there is evidence to indicate that man-biting ticks are similarly capable. There are many varieties of such ticks, and they are widely distributed over the world, America having numerous distinct specimens.

Ticks, or wood-lice, belong to the order Acarina and to the family Ixodidæ and are allied to spiders and itch-mites (Acarus Scabiei) and in some of their habits they resemble bed-bugs (Cimex lectularius). So far as known they take no vegetable food, being blood feeders. Concerning the life habits of ticks Major Charles Mason, Surgeon, United States Army, writes as follows: "The newly hatched larva, which has six legs, ascends to the stem of a plant and attaches itself to some passing animal, sucks a meal of blood, drops off to the ground, moults, and having acquired another pair of legs, again ascends the plant stem, attaches itself to an animal, fills itself with blood, and dropping to the ground again, lays thousands of eggs, which in due time become young ticks." (International Clinics, 1904, Vol. 2, Series 14, page 18.)

Two varieties of tropical ticks in particular, possibly identical, have long been suspected of conveying disease to man. They are Argas Persicus, native of Northern Persia, and Argas moubata, native of Central and Southern Africa. Dr. Livingstone, the

famous African explorer, was first to describe a disease which he attributed to the tick and which he encountered in Portuguese South Africa. More recent reports, by other travelers and medical men, upon the affection described by Livingstone, correspond in a general way with his description. The Persian and African ticks are similar in habit, both being nocturnal in their biting and both infesting old houses. The natives recognize the bite of the parasite as productive of both local inflammation and of fever, more or less severe and sometimes fatal. Certain bird and man-infesting ticks are known to be long-lived, surviving for years and living for months without food. Ticks are alleged to have caused much discomfort, at least, to soldiers during the recent Boer War, in Africa. Daniels describes the symptoms of tick fever, as observed by him in Africa, as including an incubation of five or ten days, the bite of the parasite producing a small lump which disappears in a day or two. Abdominal pain, vomiting, diarrhea, chills and fever, ranging from 101° to 102.3° Fahrenheit, were observed. Dysenteric symptoms were also said to occur occasionally. He found no blood organisms present upon three examinations.

Manson, in his Lane Lectures, in 1905 (Page 186–187), described a case of recurring fever studied by him in London. It was accompanied by spirillar blood-infection and recurred at intervals of two weeks and originated at Gibraltar. He questioned the identity of the case (as one of ordinary relapsing fever due to Spirillum Obermeieri) on account of the attacks of paroxysmal fever occurring every fortnight. In connection with the case he made the following remarks:

"Recent observations in British East Africa and in the Congo have shown that a spirillar fever known as 'Tick Fever,' is by no means uncommon in those parts of Africa. As yet, information on the subject is scanty; but it is conceivable that some of these African spirillar fevers are of the same nature as that which I saw at Gibraltar, and recur not two or three times only, as in the European disease, but seven, eight or more times. If this be so then it is possible that such cases invalided home may turn up

from time to time in temperate climates and trouble the conscientious diagnostician."

He suggests that in all cases of bi-weekly recurring fevers careful blood examination, using stained films, be made for spirilla.

F. C. Wellman, of Angola, West Africa, in an article presented to the American Society of Tropical Medicine (Transactions of 1905) and published in "American Medicine," July 22, 1905, discusses the relation of relapsing fever to tick fever in Africa, and reports several observed cases of a paroxysmal, tick-produced

Fig. 94.—Spirillum of relapsing fever.
Sketch from a stained specimen. (Williams.)

fever, clinically like relapsing fever in temperate countries and associated with the *spirillum obermeieri* in the blood. These spirilla are sometimes scarce in the blood and therefore apt to be overlooked. The symptoms observed were pains in the head, back, chest and limbs, splenic tenderness, vomiting, conjunctival injection, and febrile paroxysms of several days' duration, during which time the spirilla are found in greatly increased numbers in the blood.

There is room for strong suspicion that tick fever may be re-

lapsing fever, a disease not hitherto generally grouped with tropical diseases.

A fatal cattle fever of the Southern United States, "Texas Cattle Fever," has been shown, through the researches of Smith and Kilborne, to be due to an intracorpuscular blood parasite, which is conveyed from one infected animal to another by ticks. This blood parasite—pirosoma bigeminum—has been sufficiently studied in its extracorporeal existence to permit of definite statements concerning its evolution. The blood parasites are sucked into the stomach of the cattle tick (Boophilus bovis) and infect the eggs of the tick, with the result that when hatched the young ticks are at once capable of infecting cattle with pirosoma bigeminum, which they do through their bites when they attach themselves to suck the animal's blood.

While we have no similarly established series of facts concerning the transmission of "Tick Fever" from man to man, analogy and the modern knowledge of the agency of insects in the transmission of human disease have led to speculation and to a search for facts.

Concerning the American affection, "Rocky Mountain Spotted Fever," recently proved to be transmitted by wood-ticks, and therefore called "tick fever," the investigations of Ricketts and King in the United States are interesting. The reports of these experiments, incomplete as yet, will be found in the "American Medical Association Journals" for July 7 and August 4, 1906, and in the "Public Health Report" of July 27, 1906.

Manson refers to the disease under investigation in his "Tropical Diseases" as "Spotted Fever of the Rocky Mountains." Its peculiarities include a limited season—April to August—a restricted geographical distribution—Montana, Idaho, and Wyoming, U. S. A.—and a rather definite clinical course marked by sudden onset, continued fever, aching and a purpuric eruption, general in distribution but especially common in the scrotal regions, where gangrene sometimes follows.

The disease has been known for something more than twenty years but was only carefully studied recently. Wilson and Chowning originally advanced the theory of wood-tick transmis-

sion in this disease, and they also believed that they observed a distinctive hematozoal parasite in cases of Rocky Mountain Spotted Fever. In the first view they have been abundantly justified by the experiments of Ricketts and King but these observers, as well as Stiles, Welsh and others, failed to confirm their observation of a distinctive blood parasite.

The conclusions from the experiments of Ricketts and King during the current year—1906—establish the following facts: The disease has been successfully transmitted to guinea pigs and monkeys by inoculations of defibrinated human blood from affected persons and it has also been conveyed from guinea pig to guinea pig through female ticks, which were permitted to bite and feed upon diseased animals for two days and later upon healthy ones, establishing the disease in the latter animals after about three days' incubation. In the monkey the symptoms closely resembled those in man. One animal died upon the ninth day and its defibrinated blood was injected into another monkey which developed distinct clinical evidences of the disease, including the hemorrhagic eruption. Doctors King and Ricketts both produced the disease in monkeys and guinea pigs—using both subcutaneous and intraperitoneal injections of human blood. All the experiments were rigorously controlled.

Ricketts, under date of August 4, 1906, writes as follows:

"Hasty conclusions as to the question of tick transmission in relation to the infection of man are, by all means, to be avoided until such time as the experiments can be repeated and the life-history of the infection worked out more thoroughly."

CHAPTER IV.

EPIDEMIC DROPSY.

Another disease of undetermined classification, and one, likewise, concerning whose distinct existence there is considerable doubt, is that described by Manson as Epidemic Dropsy. Following Manson, Le Dantec describes the condition as a distinct disease entity, reserving his judgment in the matter, however.

No cases of epidemic dropsy have been observed in the American tropics as yet, according to the Report of the Surgeon-General, United States Army, for 1905.

Manson's description, following McLeods, is that of a disease remarkably like beriberi, and he admits that many Calcutta physicians look upon the condition as true beriberi. As described, Epidemic Dropsy occurs in Calcutta and other Indian cities and (as an importation), in the island of Mauritius. McLeod described it as an epidemic occurring in cool weather and disappearing with heated conditions and states that it first appeared in Calcutta in 1877, and thereafter annually during the cool months in 1878, 1879 and 1880.

Imported to Mauritius in 1878, it destroyed 729 lives, attacking one coolie in every ten and showing a mortality of between two and three percent. In Calcutta the mortality ascribed to epidemic dropsy was estimated at from twenty to forty percent., Europeans escaping the disease. Another small epidemic was reported from Calcutta in 1901.

The principal symptoms described by McLeod are, dropsy —local or general; fever (an almost constant symptom); diarrhea and vomiting; nervous symptoms—chiefly sensory (a few cases in which paralytic symptoms developed being observed); a multiform exanthem of the face, body and limbs; cardiac arrhythmia, with murmurs and dyspnea, and the evidences of peri-

cardial effusion and cardiac dilatation; pleural effusion; and fatal edema of the lungs.

The postmortem evidences of the disease corresponded with the clinical symptoms and were inconclusive.

In view of the occurrence of nearly all these cardinal symptoms in beriberi, as well as the suggestive facts as to places and persons affected by epidemic dropsy, and especially in view of the modern classification of beriberi, one cannot resist a strong suspicion that epidemic dropsy is a manifestation of epidemic beriberi. The two nonconforming symptoms, an exanthematous eruption and fever, might easily be explained by intercurrent dengue or other disease. As a matter of truth it seems that the facts with regard to the few epidemics of record are too incomplete and unconvincing to warrant the assumption that such a tropical disease as Epidemic Dropsy exists.

CHAPTER V.

TROPICAL ULCER.

Synonyms. Oriental Sore; Biscra Boil; Biscra Button; Aleppo Boil; Delhi Boil; Bagdad boil; Bouton D'Orient.

Definition. Recently the name tropical ulcer has been proposed for the condition generally known as Oriental sore, and so long as a distinct disease is recognized and a specific ulcerating granuloma peculiar to the tropics and with distinctive features which permit of diagnosis, is understood, the newer term should be used.

The term Oriental sore, aside from being inelegant, is no longer appropriate, the disease for which it stood having been encountered outside of the Orient. The numerous local appellations are manifestly unscientific. On the other hand, the newer designation has disadvantages. In my experience as a military surgeon in the West Indies and the Philippines I have repeatedly seen upon the sick and wounded reports the term "tropical ulcer" when no such disease as the one under discussion was meant. Syphilitic ulcerations, varicose ulcers and pemphigus lesions have, within my personal knowledge, been described in official reports as "Tropical Ulcers." Tropical ulcer, as here understood, is a specific, inoculable skin lesion which develops from a papule into an indolent ulcer, which persists for months, and after healing leaves the subject, to a decided degree at least, immune to further inoculation. Until further studies in etiology clear up the causation and permit the selection of a scientific name for this condition, the term "Tropical Ulcer" will serve.

Facts of Geography and History. Tropical ulcer occurs widely throughout the tropics, including Africa, the Mediterranean Islands, Asia Minor, Persia, Arabia and India. Lately cases of the disease have occurred in the Philippine Islands. It is also encountered in Brazil and probably in the West Indies, and it

may prove to be co-extensive with the American tropics, as well as with the Oriental tropics. It is more prevalent in cities than elsewhere, probably on account of the more intimate contact of large numbers of people. In the Indian cities of thirty or forty years ago, prior to the introduction of European sanitary methods, it was far more common than at the present day. Manson cites the fact that in 1864, from forty to seventy percent. of the Europeans resident in Delhi, India, suffered from the affection. In Bagdad residents and visitors are reasonably sure to acquire the ulcer during certain periods of the year. Whether this seasonal prevalence has anything to do with the prevalence of certain flies or insects is purely suppositious. The influence of race is negatived by the occurrence of the ulcer in Europeans as well as natives. It is also claimed that dogs, horses, camels, and other domestic animals, acquire typical tropical ulcers and that the disease is communicated by inoculation from animals to man. Contact, direct or mediate, must, therefore, be taken into account as a possible manner of communication. At various times micrococci of several kinds have been discovered in the discharges from tropical ulcers.

Upon isolation, culture and inoculation of these several bacterial bodies, after the manner of vaccination, no typical lesions resulted; while inoculations with the unaltered discharges from tropical ulcers produce, as is well known, similar lesions in the person inoculated. This fact strongly tends to disprove the causative character of the micrococci studied. The bacteria are probably incidental to pus infections and grafted upon the tropical ulcers.

In 1885, Cunningham, and in 1901, Firth, discovered bodies which they believe to be parasitic, in the bases of tropical ulcers, and the name Sporozoa Furunculosa was given to these bodies. In 1903, H. Wright, an American observer, reported the finding of certain protozoa-like bodies obtained from a tropical ulcer (Delhi sore). English observers generally were convinced from the descriptions and photographs submitted, and from confirmatory experiments in India and elsewhere that these bodies are identical with the Leishman bodies. They have attempted to interpret

their presence in tropical ulcers as causative and at present the weight of opinion points to the identity of the Wright and Leishman bodies. (See Chapter II, Part III.)

Etiology and Prophylaxis. Studies are now being conducted in different parts of the world looking to the clearing up of the pathology of tropical ulcer. In the preceding chapter on febrile splenomegaly I purposely avoided reference to the discovery of the Leishman bodies in the granulations of tropical ulcer, for there is still insufficient evidence to definitely connect febrile splenomegaly and tropical ulcer. It is, however, a fact that Leishman bodies, or bodies indistinguishable from them, have been found in sections of papules and ulcers of the skin in clinical tropical ulcers with a fair degree of constancy, and Stephens and Christophers (page 376, "The Practical Study of Malaria and other Blood Parasites") venture the following statements concerning Leishman bodies:

"We have thus in an infection caused by these parasites two processes—1. 'Tropical Ulcer,' a local invasion of the nature of a granuloma. 2. A systemic infection of the nature of a septicemia, involving chiefly the visceral endothelia."

Apparently, febrile splenomegaly does not occur in at least the vast majority of cases of tropical ulcer, a condition so common that in some countries the affection, nonfatal, and practically benign, is present in seventy-five percent. of the inhabitants. Constitutional invasion of the spleen and liver, then, from tropical ulcers, is not only unproven but improbable. If, on the other hand, purely local skin infections with Leishman bodies (tropical ulcer) prove to be due to the identical parasites of tropical febrile splenomegaly, Manson's suggestion that a reduction of virulence has occurred in the passage of the parasite through some animal besides man, may be correct.

Concerning the immunity conferred by one attack, it is interesting to learn that the Jews of Bagdad, recognized that tropical ulcer is inoculable and autoprotective years ago, and that they practised the vaccination of their children upon some portion of the body covered by clothing, in order that their faces and other

exposed parts of the body be not disfigured by the ulcers and the resultant scars.

Prophylaxis. Prophylactic indications must await further investigation as to the mode of communication of the disease. Inoculation, as practised by the Jews, would seem to suggest vaccination, and it is possible that an attenuated virus, capable of protection and freed from pathogenic micro-organisms, may be developed.

Pathology. The pathological anatomy of tropical ulcer, beyond what has already been indicated, needs to be cleared up by further study.

Symptoms and Treatment. Tropical ulcers usually number but one or two to the individual, but they may be as numerous as five or ten, and, very exceptionally, they may reach the number of twenty. They appear chiefly upon the uncovered parts of the body, the face, arms, hands, and legs. The initial lesion, a small red spot, becomes a papule or nodule, and this nodule slowly grows in size and becomes covered with a scaly crust which separates, leaving an ulcer exposed beneath. A purulent discharge from the ulcer forms a new crust and again separates, leaving an ulcer of increased size which finally becomes perpendicularly excavated or punched out in appearance, with a circumscribing area of inflammation. The ulcer eventually heals by granulation after months, or even a year or more, leaving a depressed pink or white scar which may further contract and disfigure the subject, should it be upon the face.

These occurrences may be grouped into four periods: First, the period of incubation; second, the period of the papule; third, the period of ulceration, and fourth, the period of cicatrization.

The period of incubation is variable, and is believed to extend from four days to months. That the shorter incubation period exists, is proved by the occurrence of the lesions in travelers within a week after their arrival in the district in which the disease prevails.

When artificially inoculated, the incubation period may be as brief as one week.

The possible complications are numerous and include erysipelas, phagedenic extension, lymphangitis, and septic intoxication. It will be apparent that these complications are chiefly the results of super-added infections. The average diameter of uncomplicated tropical ulcers varies from three-quarters of an inch to one inch.

Treatment. Surgical procedures, such as the destruction by cautery, or the extirpation with the knife, of the papule or the ulcer itself, naturally suggest themselves, and inasmuch as the duration of the four stages named often approximates a year, such suggestions may be seriously considered. Phototherapy should be investigated and the lesions, in any event, should be treated antiseptically. Aseptic dressings should be kept applied by bandages, adhesive straps, or by collodion dressings. Doubtless these precautions alone will hasten healing and limit cicatrization and deformity.

Constitutional treatment is unnecessary unless complicating conditions, such as anemia and septic intoxication exist.

Diagnosis. In arriving at a diagnosis the objective clinical appearances and the clinical course which have been described should be taken into consideration. The mode of development, the fact of residence in an endemic area, and the benign character of the affection should also be considered.

If present indications are fulfilled we may have a microscopic diagnostic method of certain value, in the discovery of Leishman bodies in the granulations which occur in tropical ulcers. The technique of this search has been given in the chapter upon tropical febrile splenomegaly. (See Laboratory Detection, Chapter II, Part III.)

CHAPTER VI.

YAWS.

Synonyms. Frambesia; Pian; Polypapilloma Tropicum.

Definition. Yaws is a chronic eruptive disease of the tropics, inoculable and highly contagious, and is characterized chiefly by numerous papules and nodular outgrowths upon the skin which undergo ulceration and present a crusted, raspberry-like appearance; and also by indefinite and inconstant systemic symptoms, such as fever and anemia. One attack confers an imperfect immunity.

Although grouped by many writers with the diseases of uncertain classification, the uncertainty is chiefly with regard to the infecting principle. Yaws is now conceded to be a distinct affection, but whether or not it is more than a local cutaneous disease is an unsettled point. The pathology and classification of tropical skin diseases has been in an extremely chaotic state until recent years, and the confusion concerning the identity of a few diseases which occur in numerous parts of the tropical world, under many names, is still great.

The contention in favor of the identity of Yaws and syphilis, which has for years been advanced by certain eminent observers, has now, by rather general consent, been definitely abandoned. The two diseases are certainly not identical.

Facts of History and Geography. The disease is known to be more or less common upon the continents of Africa and Asia, and in the following countries and islands: Ceylon, China, Java, Borneo, the Malay Peninsula, and the South Pacific Islands generally (especially the Samoan and Fiji groups). It is also known in most of the West India Islands, and probably occurs on the American mainland. According to the report of the Surgeon-General, United States Army, for 1905, it had not been

encountered in the Philippines up to the time of publication, but subsequent information shows that Yaws must be included in the list of diseases of the Philippine Islands (Strong in Philippine Journal of Science, page 9, January, 1906). Those who contend that Yaws was originally an African disease have a difficult proposition to prove, although it is generally believed to have been introduced into the West India Islands, during slavery days, by the blacks.

Etiology and Prophylaxis. While we are in ignorance as to the infecting or contagious principle we have abundant data to show that Yaws is only distributed by contagion and we are, therefore, able to prevent or control its spread. The necessary contact to cause infection may be either direct or mediate, buildings, clothing, etc., temporarily giving lodgment to the contagious principle. Whether the contagious principle be bacterial or animal in character is as yet an undetermined question. In either case it is probably a microscopic organism. Various micrococci have been isolated from the exudations of Yaws and some of them have been cultivated and inoculated for experimental purposes, but invariably with negative results so far as the productions of Yaws is concerned. The disease is always an acquired one, heredity having been shown to be entirely negative in its influence. Age, sex, and occupation are probably negative also, except in so far as they promote contact, and, therefore, contagion. Males, as a matter of fact, suffer from Yaws more frequently than females. Caucasians, Malays, Mongolians, Negroes, and Indians are equally susceptible.

Pathology. The absence of pathologic changes in the internal organs of individuals suffering with Yaws is strong evidence in favor of the view that the disease is a purely local one. Whenever pathologic changes have been encountered in persons dead with the disease, intercurrent maladies or infections have been shown to be present. The pathology of the nodular and ulcerating skin lesions in Yaws requires further study. The lesion seems to be an ill-developed granulomatous growth in which imperfect development of the cells of the interpapillary epithelial layers and of the

cells of the horny layers, together with leucocytes and micrococci, form a stratified crust.

Symptoms and Treatment. The incubation period in Yaws varies from two weeks to several months and seems to be slightly shorter in experimental inoculations. It is both alleged and denied that prodromal systemic symptoms precede eruption. The initial lesion appears as a small papule which increases to the size of a cherry or raspberry. The papular elevation is conical from the first and its apex early takes on a yellow, cheesy appearance, in reality a point of necrosis. This conical growth becomes flatter and studded with several yellowish points of necrosis. When ulceration is established, a thin, offensive, yellowish fluid is discharged and hardens into a crust. Upon the removal of these crusts the characteristic raspberry appearance of the nodules appears. The Yaw when fully developed, is an elevated, hemispherical nodule of about three-quarters of an inch in diameter. Occasionally the lesion is larger, but it is more often smaller. Yaws may be distributed widely over the body or they may be localized in a small area. Most observers assert that these lesions do not occur upon mucous membranes. The face, the extremities, hands, feet and limbs, and the genital region are frequently affected. The healing process may begin at the centre of the lesion, in which case a peripheral, circular, elevated area of granulation is seen. This appearance has suggested the term "ring-worm Yaws." Lesions in various stages of healing are usually present at the same time. The resulting scars are usually superficial. The duration of the disease varies from two months to a year or more, and successive crops of Yaws may occur. Various pyogenic infections may become implanted upon the Yaws but pus is not usually present in any amount. During the period in which the nodule is forming, considerable itching is complained of but the developed Yaw is almost painless. Fever during the eruptive period and enlargement of the lymphatic glands are frequently observed, and articular and muscular pain, rheumatoid in character, are common.

Treatment. Internally, iron, potassium iodide, and mercury

are believed to hasten the progress of the healing process. Arsenic is also advocated for the cases in which the eruption is persistent. Antiseptic dressings, and the application of some healing anti-pruritic and antiseptic dusting powder or ointment are advocated. Ulcerations should be treated on surgical principles and tonics should be given until the health is restored.

When ulceration extends into the tissues underlying a Yaw, a chronic excavated ulcer may develop which may persist for years unless surgically treated. Unless phagedenic sloughing or ulceration supervene, Yaws is a comparatively harmless disease. The death rate in the West Indies, in a large number of cases observed, was about two percent. When phagedenic processes are engrafted the mortality is greatly increased.

Diagnosis. Having abandoned the view that Yaws is modified syphilis, we must be prepared to diagnose between the two diseases. This usually should not be difficult. On account of a response obtained from administering iodide of potash and mercury in Yaws, as well as in syphilis, the therapeutic test is of little value.

A condition likely to be mistaken for Yaws is the disease known as *Peruvian wart* (*Verruga Peruana*, or Carrion's disease), a South American disease encountered in Peru and in the Andes at altitudes above 3000 feet. Formerly considered as a modified form of Yaws, it is now looked upon as a distinct disease belonging to the infective granulomata. The systemic manifestations, consisting of fever, rheumatoid pains and hemorrhage, are more severe than those observed in Yaws. In appearance the lesions of Verruga Peruana are variable. They are fungating tumors somewhat resembling warts and the raspberry-like lesions of Yaws. This disease has a very limited geographic distribution so far as our present information goes. A Brazilian disease known as *Frambesia Brasiliania*, or *Boubas*, also bears some resemblance to Yaws. It is a chronic condition of ulceration rather than one of outgrowth, and the lesions appear on the mucous surfaces as well as upon the skin. The initial lesion is a pustule.

CHAPTER VII.

TROPICAL SLOUGHING PHAGEDENA.

Tropical Sloughing Phagedena is a condition of superficial gangrene rather common in the tropics and has been described by several writers under this name. Whether or not the condition constitutes a distinct tropic, pathologic entity is questionable.

Many practitioners of medicine and surgery, with extended experience, have doubtless encountered conditions corresponding clinically with *Tropical Sloughing Phagedena* in the United States and in other temperate zone countries.

Essentially, the process is a superficial gangrene with a decided tendency to spread circumferentially and rapidly. This tendency, however, is limited and the areas of necrosis do not usually attain great size. The process, concerning whose causation we have no positive knowledge, occurs principally in those reduced in tissue vitality and resistance by other diseases, especially malarial or diarrheal. It is also apt to occur in areas surrounding a skin lesion, such as a punctured wound, small ulcer, or scratch. In many respects it resembles "Hospital Gangrene," now happily almost unknown, but it seems to be less fatal, less contagious and less extensive in its destruction than hospital gangrene. It may, however, be identical with this condition and should be considered infectious and contagious. Isolation should, therefore, be practised.

It is safe to assume that the condition is due to tissue invasion by some virulent pyogenic and tissue-destroying micro-organism. What this particular organism may prove to be, is speculative, no conclusive investigations having been conducted as yet. The parts of the body chiefly affected are the extremities, feet, legs and arms, these members being most exposed and liable to skin abra-

sions which may serve as gate-ways of infection for the organism. The earliest evidence of the process is the formation of a blister, which ruptures within a few hours, exposing a gray superficial necrosis beneath. Within a day the necrosis may extend an inch or more and may continue until an irregular circular area, six inches or more in diameter, according to location, is attained. The necrotic tissues, usually limited to the skin and fascia, rapidly assume a dirty yellow color and take on a sickening odor. The process may come to an end within a week, the necrotic slough being gradually separated from the healthy tissues beneath. Occasionally muscles, nerves, and blood vessels are involved in the necrotic process, and joint invasion may occur. In this event hemorrhage, deformity, or even loss of the member, may result. The systemic symptoms are usually mild. They may, however, be severe, and even result in death.

The **treatment** should be two-fold in its object, and should be directed toward the support and upbuilding of the patient, and towards the destruction of the causative micro-organisms. Diet, generous feeding and tonics, answer the first indication, and surgical measures the second. Extirpation of the sloughing lesion as soon as its character is recognized, and a thorough cauterization of the exposed tissues, under anesthesia, should be employed. Manson recommends, "That the patient be put under chloroform and the slough thoroughly dissolved off by the free application of pure carbolic acid, a piece of lint on a stout stick being used as a mop for the purpose. Thereafter the limbs should be elevated, and placed under some improvised irrigator, from which a weak, warm, antiseptic solution should continuously trickle over the now clean surface. If the phagedenic action recur, the carbolic acid must be promptly reapplied as often as may be necessary. On healthy granulations springing up the ulcer is to be treated on ordinary principles."

CHAPTER VIII.

MYCETOMA.

Synonyms. Madura Foot; Fungus Foot of India; Pied De Cochin.

Definition. Mycetoma is a tropical disease associated with and probably caused by a vegetable parasitic fungus of the Actinomyces group—*Streptothrix Mycetoma* (or, S. Madura). It is usually an affection of the foot but occasionally occurs in the hand, knee, shoulder or other exposed part of the body. The disease is characterized by great swelling and deformity of the affected member and by a gradually extending inflammation, beginning upon the surface and penetrating to the deeper tissues, including the bones as well as the soft parts, and terminating in necrosis, an oily degeneration, and the formation of a system of cavities and sinuses, intercommunicating and extending to the surface. These cavities and sinuses are usually filled with and discharge an oily sero-purulent fluid in which are suspended small masses, either pale or black in color and round or coarsely granular in form, resembling grains of iodoform or gun-powder.

Facts of Geography and History. Mycetoma is widely distributed throughout the tropical world, including the American tropics, and has been encountered in a few instances in the United States. China, India, Egypt and tropical Africa, as well as South America, present cases of Mycetoma. It is pre-eminently a disease of bare-footed people and, possibly on this account, it is more common in the country than in the city. It takes its popular name, Madura foot, from Madura, India, where it is very prevalent. It occurs more frequently in warm countries because of the habits of the natives (bare-footed) and a special susceptibility on the part of dark skinned people. Many cases have been reported from Panama.

Although the disease was first observed nearly two centuries ago, no scientific studies of any importance concerning it were made prior to 1860. During the fifteen years following this date Van Dyke Carter, in India, contributed important descriptions and conducted experiments showing the parasitic nature of the disease.

Etiology and Prophylaxis. Streptothrix Madura closely resembles the ray fungus, Actinomyces. Laveran believes that there are two varieties of S. Madura, both of them distinct from the ray fungus of cattle. In infection with one of these varieties minute granular masses, black in color and resembling grains of gun-powder, are discharged from the sinuses before mentioned. In the other variety identically shaped granules, yellow or gray in color, are discharged and some observers have also noted granules pinkish in color. If a number of these granules become agglutinated the discharged mass may be round and as large as a pea. The method by which the fungus gains entrance to the foot is not known, although it has been suggested that the parasite exists upon some tropical plant and enters the skin through an accidental abrasion or puncture. If this supposition be proved correct the natural prophylactic method will include the wearing of shoes.

Pathology. Section through a mycetomatous foot reveals an oily gray mass in which the normal appearance of bones and soft tissues is lost, the various elements being infiltrated with an oily granulation tissue and marked here and there with cysts which may measure an inch or more in diameter. These cysts are united by sinuses which are filled with a brown, white or yellowish, cheesy material, containing the granular particles which are discharged. In the white variety this material suggests fish-roe. The process usually begins in the sole of the foot and does not commonly extend above the ankle and it may continue for years without becoming diffused through the body. The discharge from the sinuses, which are lined with a firm membrane, is sero-purulent in character and rarely bloody. These sinuses appear in a perfect network uniting the various cavities and the surface of the foot. An obliterating endarteritis has been demon-

strated in the blood vessels. The tissue changes in mycetoma are peculiar to this disease, no similar changes being known in any other affection.

Symptoms and Treatment. The earliest sign of mycetoma is the appearance of a small, round, tuberous outgrowth upon the skin, usually upon the sole of the foot, which gradually softens and begins to discharge the characteristic oily, sero-purulent fluid described. It may require several months for this condition to develop. Other similar swellings appear and continue to do so, the sinuses rarely healing. The diseased member increases to twice its natural size and the natural contour is generally lost. A probe passed into the orifice of one of the sinuses, which orifices are crater-like in appearance, advances practically without resistance, pain or hemorrhage. The discharge may be very offensive. The chief inconvenience to the victim is the presence of a swollen, offensive, useless member, the pain being usually an insignificant matter. If the foot be the part affected the leg gradually wastes above it. The disease sometimes extends to the bones of the leg, or, in case the hand is the diseased member, to the forearm, but generally the disease shows a remarkable localization. The duration of mycetoma may be five, ten or even twenty years, unless some surgical complication shorten the life of the patient.

Mycetoma may properly be considered as a purely surgical disease, particularly from the viewpoint of *treatment*, the only constitutional evidence of the disease being the cachexia and anemia which attend long continued suppuration. Septic infection and lymphatic swelling sometimes complicate the disease. Once developed, the condition is incurable and amputation through sound tissues, well above the diseased part, should be performed. In the early stages less extensive operations, with the knife or curette may be undertaken.

LABORATORY DETECTION OF STREPTOTHRIX MADURA (MYCETOMA).

The granules found in the discharge represent masses (clumps) of mycelium. They are of caseous consistence and insoluble in

liquor potassa and in acetic acid. With a needle remove one of the peculiar colored particles found in the discharge; place it upon a glass slide and gently drop upon it a cover-glass. Under a medium-power lens the appearance is that of a globe of the characteristic color, black (melanoid) or pale (ochroid), either white, yellow, or (rarely), pink. Pressure upon the cover-glass causes the dense clumps, consisting of filaments of mycelium, arranged radially, to appear. The ends of the radiating filaments are swollen, giving them the so-called club shape. A $\frac{1}{5}$ dry lens or a $\frac{1}{12}$ oil immersion lens may be used. Staining is unnecessary, but in either cover-glass preparations or in sections beautiful stained preparations may be made. For smear preparation, fix a smear and stain with an ordinary carbol-fuchsin solution. Partly decolorize with fifty percent. alcohol and wash thoroughly in water. Dry and mount in Canada balsam.

The organism is stained by the Gram method.

S. Mycetoma is aërobic and grows in ordinary media, but not always readily. It grows well in a simple potato bouillon, (20 grams of potato to 1,000 grams of water) and also in glycerine-gelatine medium. It forms spores and does not liquefy gelatine.

It grows in association with pyogenic micrococci and will grow upon steamed potato in small white elevations which, after a month, take on a rose color, or even a red color if the potato is very acid. In bouillon cultures the growth appears as floating flocculi which grow to masses of the size of peas in a month. These masses also take on a rose color after about two months. Milk is not coagulated by the growth.

CHAPTER IX.

CLIMATIC BUBO.

I desire to make brief reference to a few clinical conditions encountered in some of the American tropics which do not fall within any of the classified groups. The first of these is a condition of adenitis commonly described as *Climatic Bubo.*

Scheube has described, in his "Diseases of Warm Countries," a nonvenereal swelling of the lymphatic glands, usually associated with fever and affecting principally the glands in and about the groin, either on one or both sides of the body. This somewhat ill-defined condition is said to occur among tropical sailors of several nationalities and to be epidemic at times and especially aboard ships. Cases have been reported in the German, British and American Navies in different parts of the world. Rather recently "Climatic Bubo" has been described as prevailing in the Panama Canal Zone. During service in Cuba I encountered glandular enlargements of the groin accompanied by fever, and in a few cases by suppuration, in which histories of syphilis, or venereal disease of any kind, were entirely lacking. The term Climatic Bubo, however, as applied to these conditions, seems to be entirely inappropriate, there being no evidence whatever to indicate that climate bears any causal relation to the condition. It has been suggested that these glandular enlargements may be expressions of Bubonic plague—true Pestis Minor—and also that they represent a glandular expression of Dengue. The more probable explanation, in the majority of these cases, is that the glandular swelling is the result of nearby skin infection, introduced perhaps through a microscopic lesion or abrasion, or through the agency of some biting insect or fly. The course of the disease, if it may be so designated, is usually a sluggish one and may terminate either in complete resolution

or in suppuration. If evidence of the later occurrence appears surgical treatment should be instituted; either incision or excision. If the latter operation is chosen one should be prepared to perform an extensive operation, as all the affected glands should be removed. I have removed as many as a double handful of enlarged lymph glands, varying in size from that of a pea to a walnut, in a case in which the external evidences suggested a far less extensive adenitis. These glands were in various stages of suppuration and liquefaction. Discharging sinuses are apt to follow an incomplete operation. If suppuration does not occur, the condition should be treated by rest in bed, application of the ice bag, or shot bag, by inunctions of iodine or mercurial preparations, or by bandaging. The general health must be looked to, especially if suppuration be present, in which case iron, and other tonics, and a liberal, nourishing diet should be administered. Fever and other systemic manifestations should be treated symptomatically.

Studies of the blood and pus, conducted to identify climatic bubo with pestis minor, have recently been conducted in China with negative results. (Journal of Tropical Medicine, January 2, 1905, Clayton.)

The eosinophile leucocytes have been observed to be increased.

CHAPTER X.

AINHUM.

Another disease of the unclassified group is that known as **Ainhum.**

It is an endemic tropical disease, occurring both in the Orient and in the Occident, and affecting, chiefly, negroes and the natives of India, although, as has been recently shown, it is not strictly limited to these dark skinned people.

The English equivalent of the term Ainhum is "To saw."

The disease is also known as **Dactylolysis Spontanea.** It is an essentially chronic affection of undetermined causation and consists of a slow, spontaneous amputation of the toes, either one or more, at about the digital plantar fold. This spontaneous amputation generally occurs in the little toe, but in some rare cases the second, third, and even the great toes are lost. Next in frequency to the little toe, the fourth one is usually affected. In some cases, the affection is symmetrical; in many cases, however, it is not so.

Various theories as to causation have been expounded. One of the most popular ones is that the lesion is a trophic one, secondary to some disease of the nervous system. Another view is that Ainhum is a form of scleroderma. It has also been ascribed to infection wounds of the bare feet acquired in walking; and to the wearing of rings or ligatures about the toes. Perhaps the most strongly supported view is that Ainhum is a manifestation of leprosy. Recently, F. C. Wellman, of Angola, West Africa, has collected evidence adverse to the theory of leprosy in Ainhum. (Journal Tropical Medicine, Oct. 2, 1905.)

It may be said that none of the suggested theories have been, in any sense, proven. Some recent cases of the disease have been reported in the United States.

The spontaneous amputation begins as a circular furrow in the digital plantar fold of the toe. Gradually this furrow deepens, without evidence of inflammation, and a condition of dry gangrene gradually develops. The distal extremity of the affected digit becomes swollen and globular. The process of amputation may require five or even ten years, although the toe may drop off after one or two years. The process is painless and is not accompanied by any constitutional symptoms. The sensibility of the affected toe is altered but not entirely lost, at least, not until the process is well advanced. If ulceration occurs, there may be symptoms referable thereto.

Treatment consists in dividing the constricting band in the earlier stages of the disease—an effort to check the process of slow strangulation of the toe. If this fails to arrest the process, amputation should be performed either through the pedicle caused by the constriction, or by disarticulation at the meta-tarso phalyngeal joint. The diagnosis of the condition should present no difficulties whatever. The etiology and pathology are obscure and the prognosis, so far as the salvation of the toe is concerned, is bad.

CHAPTER XI.

GOUNDOU.

Another tropical disease or condition which falls well within the unclassified group is **Goundou**—a peculiar dystropic affection limited almost exclusively to the negro race and observed principally in Africa. Cases in the West Indies have also been observed and it is possible that the disease exists on the continent of Asia and in the Pacific Islands. This affection has numerous African synonyms, but the other terms applied to the condition are all equally barbaric and chiefly signify "Big Nose." The condition was first encountered in Africa and was described in 1882 by MacAlister and in 1887 by Lamprey. In 1895 the condition was again called attention to by Macloud, who found that in certain African villages the disease occurred in about one percent of the natives. It is probable that Goundou has a fairly wide tropical distribution, although the incidence of the disease is far less than indicated by the percentage just quoted. The condition is said to appear in childhood or in early adult life and consists, in its earliest manifestations, of headache and the gradual appearance of symmetric hard tumors upon the sides of the nose at about the junction of the nasal bones and cartilages. During the early days of the disease a purulent discharge occurs from the nares, but at the end of some months both the discharge and the headache subside; the symmetric tumors are persistent, however. These tumors are believed to be due to a periostitis and to represent conditions similar to exostoses. Various theories as to the causation of this strange condition have from time to time been proposed, among them are the following, as related by F. C. Wellman, of Benguella, West Africa (Journal of American Medical Association, March 3, 1906).

"1. That it is a sequel of yaws (Chalmers).

"2. That the condition is a disease *sui generis* (Braddon).

"3. That the condition is an example of atavism referable to some tribal peculiarity of the original negro stock (Strachan).

"4. That it is a manifestation of syphilis (Freidrichsen).

"5. That the tumors consist of malformations due to non-union of the nasal and frontal bones (Keng).

"6. That they are caused by the presence of larvæ of insects in the nostrils (Maclaud)."

None of these hypotheses has been proven or even made strongly probable. Wellman found that cases of goundou existed in which the possibilities of an antecedent yaws could be positively excluded. The same fact is true with regard to syphilis.

The peculiar symmetric tumors are of a firm, bony consistence and do not in any way affect the overlying skin. They may attain the size of hen's eggs or small oranges and (according to Manson) even that of ostrich eggs. The cavities of the nose are encroached upon but not to such an extent as to make nasal breathing impossible. The pathology of the condition is nearly as obscure as its etiology and further information must be collected with regard to this peculiar affection. The disease does not seem to be fatal nor attended with symptoms other than those due to mechanical obstruction of the nasal cavities.

CHAPTER XII.

SKIN AFFECTIONS.

Tropical dermatology offers a most inviting field for the student. Extended investigation will be needed, however, before anything like a systematic classification of tropical skin diseases can be presented. Skin diseases which fall quite outside of the large group of those which are but local expressions of constitutional diseases, as, for example, leprosy, syphilis, elephantiasis anp various bubonic expressions, are very numerous. A small groud which we will consider here includes **Pemphigus Contagiosus, Tinea Imbricata, Pityriasis** or (**Tinea**) **Versicolor, Pinta,** and **Miliaria.** Some of these affections are included under the popular designation **Dhobie Itch.**

This grouping is followed on account of the extensive prevalence of these diseases in the tropics rather than on account of their physical similarity. All of the diseases except Tinea Imbricata and Pinta are occasionally met with outside of the tropics, but it is believed that constant tropical conditions are necessary for the existence of these two vegetative diseases, an atmospheric temperature of less than 70° F. being incompatible with the life of the fungus in both cases.

All of the diseases except Pinta are encountered in the Philippine Islands, and in the West Indies all are observed except, perhaps, Tinea Imbricata and Pinta.

Pinta is distinctively an American disease, occurring from the southwestern United States in the north to Brazil, in the south, although certain chromogenic fungus skin diseases resembling it have been observed in Africa and also in the Orient.

Both of these diseases, it appears, may be introduced into countries where the requisite climatic conditions for the propagation of their especial fungi are present and the same facts also hold good for various other skin diseases. We will omit from

special consideration the various skin diseases of the temperate zone countries. Most of them are present in greater or less profusion in the tropics, the conditions of moisture and warmth conducing to germ proliferation, not to mention the increased ease with which skin affections may be acquired by those who wear the scanty native garments of the tropics.

PEMPHIGUS CONTAGIOSUS.

This disease is without special constitutional manifestations. It resembles Impetigo Contagiosa but differs from it in the fact that the formation of crusts, common to Impetigo, is inconspicuous in contagious pemphigus. It resembles it in its contagious character, however, and occurs frequently in barracks and institutions, and among soldiers, prisoners, and laborers. The local lesion, which occurs upon any part of the body, is distinctive, but it may easily be mistaken for Impetigo Contagiosa. It is quite as contagious but less inflammatory in character and no fever accompanies the disease as a rule. The lesion is a rapidly developing round, or oval, vesicle, becoming bullous in character, and attaining at times a diameter of three-fourths of an inch to one inch, if the circumferential exfoliation of epidermis about the original lesion be included. The lesions are usually discrete but the exudative process may often start anew at the borders of an exfoliated area. The exuded fluid is clear at first but rapidly becomes opalescent and somewhat milky, but never of very thick consistency. The crust-like formation of Impetigo Contagiosa is usually lacking, therefore. The base is glazed and red and this glazed condition persists for some time, gradually becoming pale. The disease is somewhat pruritic and scratching may convert the typical pemphigus lesion into something quite unlike the original eruption, suppuration and destruction of the deeper tissues and lymphatic involvement occurring.

Contagious pemphigus closely resembles the ordinary pemphigus vulgaris, its chief distinguishing feature being its contagious character. I have seen this disease go through a company of soldiers or troopers in Cuba, and also in the Philippines. In the

Philippine Islands, however, it seemed less contagious than in Cuba. Cases, evidently of this particular disease, were by no means infrequent, and often occurred in association with body ring-worm. The bacteriology of pemphigus contagiosus is indefinite, various pyogenic micrococci having been found both in the bleb contents and in the epidermis.

Treatment. The treatment is more or less unsatisfactory and requires painstaking patience on the part of the attendant, and control over the infected individual. Prophylaxis is important and includes the isolation of the patient, frequent disinfection of his clothing and bedding, occlusive dressings of the lesions and destruction of the soiled dressings by fire. In Cuba I found that the prompt incision of the bleb, swabbing out the cavity with pure phenol and dressing with an occlusive collodion dressing was the most efficient treatment. Each lesion must be separately dressed.

Isolation is deemed as necessary for cases of contagious pemphigus as for measles. The morbidity in certain companies was large but the mortality from uncomplicated cases was nil. The disease will doubtless be greatly reduced in barracks by insisting upon the use of boiling water in the washing of the men's clothing and bedding.

TINEA IMBRICATA.

Tinea Imbricata is an extremely common variety of body ring-worm in the Oriental tropics, Eastern Asia and the adjacent Islands, and is also encountered in the South Sea Islands of the Pacific. It has appeared from time to time in new places and may be expected to invade the Occidental tropics in time. The particular vegetable parasite or fungus, to which the characteristic lesions of Tinea Imbricata are due, is generally described as a tricophyton but its exact identity is disputed. It decidedly resembles the tricophyton at least, and may be studied by placing epidermic scales, with a drop of liquor potassæ, upon a glass slide and covering with a cover-glass, using the one-sixth inch objective or the oil immersion lens for study. The Mycelial masses are

easily discovered. Daniels recommends the use of the following improved method in which the swelling of fungus and spores caused by the liquor potassæ is avoided. Stain the epidermal scale with gentian violet aniline water for five minutes. Dry with blotting paper. Treat with Gram's iodine solution for two minutes, and dry with blotting paper. Now cover with aniline oil to which a little iodine has been added and leave until the fungus can be seen. Examine from time to time. When nearly clear treat with aniline oil and clear in xylol. Mount in balsam.

Tinea Imbricata is a dry, itching, scaling disease of the skin, exceedingly chronic and contagious. It often covers the entire body of the patient, excepting the scalp, palms, and soles, but it may be localized in spots. The individual lesion is a brownish, scaly patch or ring which expands, from an original diameter of one-fourth inch indefinitely. As the ring expands from the centre, destroying the epithelial layer, new epithelium is grown, and is in turn destroyed by a new expanding circle. These circles have been likened to the ripples produced upon the surface of a smooth body of water by a falling pebble (Manson). They average about one-fourth inch, apart and the systems of concentric scaly rings intersect each other in an interesting fashion. Naturally this appearance is diagnostic of itself. Each circle of scales shows a peripheral attachment and a central elevation. These scaly circles may simulate icthyosis but a well-developed case could hardly be mistaken for any other disease. In its early stages it might be mistaken for confluent Tinea Circinata.

Treatment. The treatment consists of the destruction of the superficial layers of the skin, in which the fungus is lodged, by iodine, pure phenol or salicylic acid in various combinations. A strong solution of salicylic acid in alcohol is effective but painful. Citrine ointment (Ung. Hydrarg. Nitratis) is useful.

PINTA.

Manson speaks of Pinta as the American equivalent of Tinea Imbricata. As the Spanish name indicates, the conspicuous characteristic of this disease is the "painted" or spotted appearance

of the skin. The disease appears to be a contagious, pruritic, desquamative affection occurring in localized skin areas which show a decided tendency to coalesce. It affects the lower classes who live in conditions of uncleanliness, and is chronic in character. There seems to be good evidence that Pinta is a vegetable parasitic disease distinct from vitiligo or Tinea Versicolor. Several investigators have found fungus growths in the skin consisting of mycelial threads and spores arranged in a network. These have been variously described and the descriptions indicate that more than one variety of fungus, with pigment-containing spores, is involved in the causation of Pinta.

The initial plaque or spot is apt to occur upon the face or hands, other parts of the body rapidly being affected. In color the initial spots may be dark, (black or blue,) or light (white or red). The variety of the disease marked by dark spots is said to spread more rapidly than the red or white variety, the violet, blue, or black pigmented fungus being more superficial in its location than the latter varieties. When once established the spot does not change in color, although the individual may present areas of pigmentation and desquamation of distinct shades or colors.

It must be admitted that our information concerning Pinta is very incomplete, although the disease is extremely prevalent in certain endemic Central American districts. The variegated individual is an object of interesting appearance. There are no changes in sensation in the colored skin areas, a distinguishing feature from the white anesthetic spots of leprosy which may otherwise resemble the lesions of Pinta. Offensive body odors are also said to emanate from the subjects of Pinta. The occurrence of white spots is interpreted by some as a simple expression of disturbance of pigmentation in the skin (leucodermia), due to a previous fungus growth in the skin, the parasite itself having died. White patches of hair also appear upon the scalp when the disease spreads to this portion of the head.

Diagnosis. The diagnosis could scarcely be mistaken, but Tinea Versicolor, the pale, anesthetic spots of Leprosy, and Vitiligo should be considered.

Treatment. Treatment should be conducted along the lines laid down for Tinea Imbricata. Prophylaxis involves the application of the same principles which obtain in other contagious skin diseases, cleanliness of body and clothing and the avoidance of contact, direct or mediate, with infected persons.

DHOBIE ITCH OR WASHERWOMAN'S ITCH.

Dhobie itch is the popular lay term in use in many hot countries to designate a number of skin diseases which affect the axillæ, the genito-crural regions and other parts of the body which come into contact with the clothing, which, in the tropics, is always of a washable material. Elsewhere I have referred to the conveyance of disease, especially body ring-worm, by means of clothing (see introductory Chapter), and the prevalence of "Dhobie Itch" in the American Tropics.

As popularly used the term includes chafing (erythema intertrigo), the various body ring-worms (tricophyton infections), pemphigus contagiosus and even prickly heat (miliaria). The term is so indefinitely applied that it has deservedly fallen into disuse among medical men.

TINEA VERSICOLOR.

Tinea versicolor, or **Pityriasis versicolor,** also known as **chromophytosis,** is a vegetable parasitic disease characterized by yellowish macular patches, chiefly of the trunk. These patches vary in color according to the complexion of the affected individual, the dark skinned races presenting areas lighter in color than the normal surrounding skin. In Caucasians the reverse is true. The yellowish, macular patches, originally of the diameter of a pea or smaller and irregular in shape, coalesce within a month or so, forming large spots of yellow or brown, and, more rarely, of a pinkish cast. The desquamation consists of fine scales and is mealy in character. There is usually itching and the course of the disease is chronic, covering months or years. The parasite producing this disease is known as Microsporon Furfur and is a

vegetable fungus which invades the corneous layer of the skin. It consists of mycelial masses of short threads and round refractive spores, which contain the characteristic pigment. These spores vary in diameter from $\frac{1}{3000}$ to $\frac{1}{9000}$ of an inch.

Treatment of the disease is much more satisfactory than that of

Fig. 95.—Tinea versicolor. (Schamberg—Diseases of the Skin.)

certain similar affections and the diagnosis may be made either from the physical appearance of the disease, or from the microscopic examinations of the scales with a $\frac{1}{6}$ inch objective, in the manner detailed for Tinea Imbricata.

Sulphur, mercury, and tar, either in the form of lotions or ointments, will be found curative if the treatment is continued for a week or so. Previous thorough cleansing of the skin, and softening of the epidermis by hot water, green soap, and friction should be secured. A 1:500 solution of bichloride of mercury in water will be found curative if adhered to.

Manson inclines to the view that **Erythrasma,** a rare parasitic disease similar in many ways to Tinea Veriscolor and caused

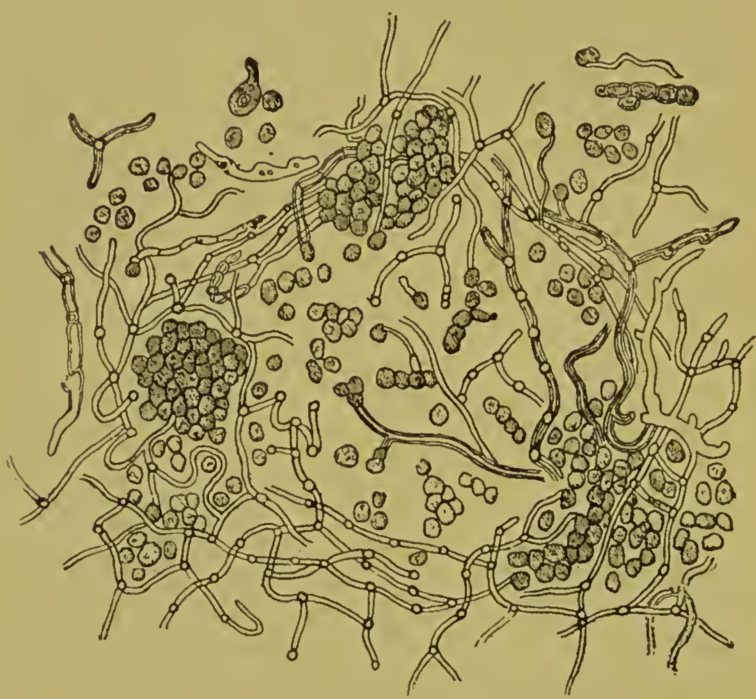


Fig. 96.—Microsporon Furfur x 700. (Schamberg. After Kaposi.) (Vegetable parasite causing Tineä versicolor.)

by the Microsporon Minutissumum, a vegetable parasite, is the cause of many cases of Dhobie Itch. The eruption resembles that of Tinea Versicolor, except that it is reddish or brownish in color. The axillary and genito-crural regions are chiefly affected, the trunk usually escaping.

The **treatment** recommended for Tinea Veriscolor will be found curative for Erythrasma.

MILIARIA.

Miliaria, prickly heat, or **lichen tropicus,** as it is sometimes called, is an inflammatory affection of the skin common among Caucasians in the tropics, both adults and children suffering therefrom. It consists of an eruption upon those parts of the body commonly in contact with clothing, and also upon surfaces prone to sweating, of small papules and vesicles corresponding with the orifices of the sweat-ducts, causing a red granular appearance of the skin. The disease follows excessive perspiration and the lesions are discrete.

The sensation of itching is frequently intolerable and leads to scratching, abrasions of the skin, a generally aggravated condition, and sometimes to pus infections.

Prickly heat is generally believed to be a nonspecific disease and therefore noncontagious, and occurs most frequently among stout persons and children. An attack of intense itching or burning may be precipitated in a quiescent eruption of prickly heat by the ingestion of hot drinks or hot food. Cold douching or bathing may aggravate the condition, and tepid solutions will be found more effective than cold ones in the treatment of prickly heat.

Treatment. Prophylactic treatment includes the avoidance of all habits which predispose to profuse sweating. Daily bathing will prevent the obstruction of the sweat-ducts (from accumulations), and the bath should always be followed by the application of a soothing dusting powder. Constipation should be guarded against.

For the relief of the intolerable itching the application of dusting powders, or of lotions, is recommended. Powdered starch, boric acid, and magnesium carbonate, well mixed in equal quantities, serve well. Carbolated lotions are often comforting. A lotion consisting of boric acid, carbolic acid, alcohol, glycerine and water is excellent and should be applied with an atomizer or mopped over the skin with absorbent cotton.

℞.	Acidi Borici	ℨss.
	Acidi Carbolici	fℨss.
	Alcoholis	f℥j.
	Glycerini	f℥ij.
	Aquæ, q.s. ad	f℥iv.
Sig.:	Apply as directed above.	

SAND FLEA BITES.

A painful skin lesion frequently encountered in the American tropics is that caused by the American sand flea (**Sarcopsylla Penetrans**), also known as the **Chigoe, Chigger** or **Jigger.** It is a brown flea closely related to the common flea (Pulex Irritans) and measures from 1 to 1.2 mm. long. Both males and females

Fig. 97.—Gravid female sand flea—magnified. (Braun after Moniez.) (Tyson's Practice.)

bite but the female only penetrates the skin, burrowing obliquely into it after impregnation and expelling her eggs into the external world from this situation.

This insect, originally native of America where it abounds in the Southern part of the United States, Central America and South America, has been imported into Africa and during the last thirty years has overrun the continent, having been originally introduced into West Africa from Brazil.

The insect infests such domestic animals as dogs and pigs also. It is most common in sandy places and the troops encamped

in the Southern United States during the Spanish war suffered considerably from its ravages. When the female attains lodgment in the skin, the tumor or edema, caused by her egg-distended body, is often as large as a pea. Pustulation and ulceration may supervene and a serious surgical condition may be set up, painful and even threatening to life, if pathogenic bacteria enter the burrow caused by the sand flea. The most frequent sites of penetration for the female chigger are the skin of the feet and hands,

Fig. 98.—Young female—magnified. (Braun after Moniez.) (Tyson's Practice.)

the toes and soles of the feet being especially affected in bare footed persons. The lesions are either single or multiple and may be counted by the hundred at times.

The treatment consists of removal of the insect, either alive or after killing it by puncture or by an application of chloroform. Extraction may easily be done with a clean, blunt needle after enlarging the external opening of the burrow. Following this an appropriate antiseptic dressing should be applied and maintained. Irritation and swelling appear from a few days to a week after the tiny insect penetrates the skin, and there should be little difficulty in arriving at a diagnosis.

LEECH BITES.

In Luzon and elsewhere in the Philippine Islands, especially in the wooded hill-country, land leeches of large size are found, and these animals proved troublesome to our troops during the Philippine campaigns. They often gained access to the legs of the marching soldier through the eyelet holes in the leggings and, having attached themselves to the skin, sucked large quantities of blood. I heard of a number of such cases in Southern Luzon, where faintness from loss of blood first attracted the soldier's attention to this most unwelcome parasite. It is probable that these leeches are allied to the land leeches of Asia and South America. The application of salt will cause the parasite to release its hold. Persistent hemorrhage from the punctures caused by the leech's bite frequently require control by pressure and the wound should invariably be antiseptically treated and bandaged.

APPENDIX.

A List of Essential Articles for Laboratory Work in Tropical Diseases.

The following list is prepared with reference to the investigation of blood, sputum, urine, feces, and water only, as described in this book, and does not contemplate the investigation of solid tissues, such as tumors, which require imbedding or freezing and section cutting. This plan is in consonance with the ideas of *utility* and *simplicity* laid down in the section on General Considerations.

For blood work, in addition to the microscope and accessories, it will often be desirable to have an instrument to determine the percentage of hemoglobin and also an apparatus for counting the blood cells and making differential counts. For these purposes the following instruments will be found useful, although these procedures are not absolutely essential for purposes of simple direct diagnosis. For estimating hemoglobin values of blood specimens an hemoglobinometer of simple pattern will be needed.

The simpler devices based upon color comparisons and requiring only a good color-sense on the part of the investigator will serve well enough. Of these devices Dare's apparatus is a satisfactory instrument, nsed without diluting the blood, but it is more expensive than the hemoglobinometer of Gower (in which dilution of the blood is necessary), or the Tallquist test paper strips. The two latter devices are cheap and satisfactory. For counting the red cells or for differential counting an hemocytometer will be required and the Thoma-Zeiss instrument, used in connection with the microscope, will be needed.

Much labor and trouble may be saved by using sterile culture-media tubes, prepared ready for use when purchased, and compressed tablets or discs of the various stains, in definite amounts, ready for extemporaneous solution. These preparations are now obtainable from reputable houses and if care is exercised to make sure of their sterility, purity and activity, satisfactory results may be obtained by their use. In view of the rapidity with which many drugs and perishable preparations deteriorate in the tropics, it will be well to use only original packages and these should be obtained in

the smallest convenient sizes. No quantities have been given in the appended list, this being a matter to be determined by the circumstances attending the work of the individual observer.

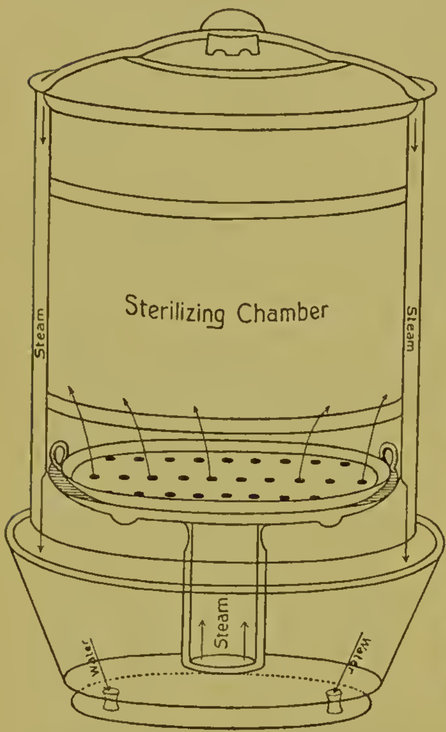


Fig. 99.—Diagram of the Arnold steam sterilizer.

Fig. 100.—Ralston new process water still. Exterior and interior.

LIST.

Portable microscope with two eye pieces and three objectives upon a triple nose-piece, $\frac{2}{3}$-inch, $\frac{1}{6}$-inch, and $\frac{1}{12}$-inch (oil immersion). Microscope fitted with an Abbé condenser and a mechanical stage.

Dropper bottle for cedar oil.

Needles or lancet for drawing blood.

Glass slides (1 x 3 inches).
Cover-glasses (round or square) $\frac{3}{4}$-inch in diameter.
} Slides and cover-glasses should be packed in oil to prevent "frosting," which rapidly takes place in the tropics, otherwise.

Forceps for holding glass slides (Kirkbide pattern).

Forceps for holding cover-glasses, Stewart or Cornet patterns (see cut on page 312).

Test-tube forceps or holders—wire.

Test-tubes (nested).
Petri dishes (double).
Flasks.
Funnels.
Glass tubing.

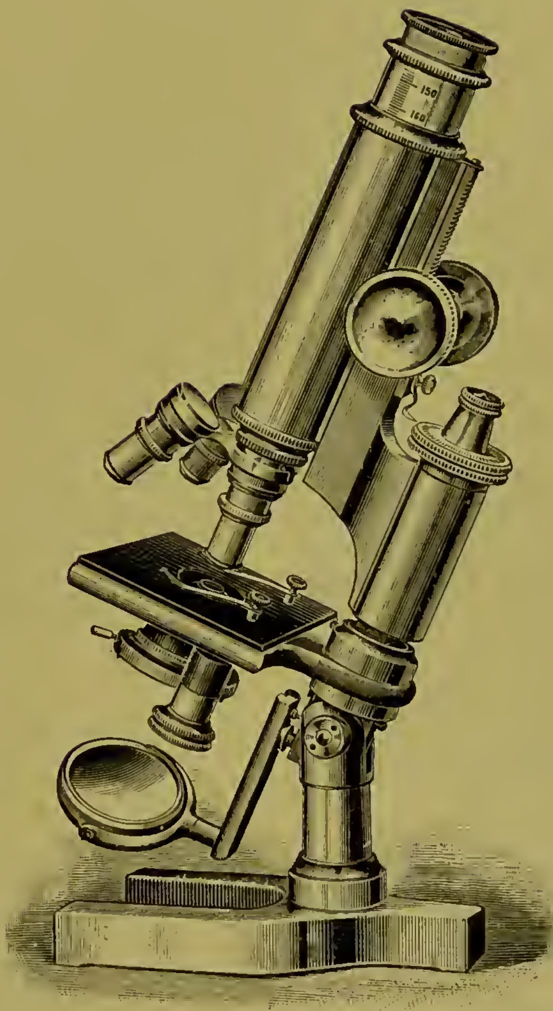


Fig. 101.—Microscope.

Glass rods.
Beakers.
Graduates (metric and apothecaries measures).
Scales and weights (metric and apothecaries weights).
Cotton-wool (absorbent and non-absorbent).

Sterilizers (steam), Arnold's. (See cut.)
Sterilizer and incubator (hot air). May perhaps be improvised.
Agate ware vessels.
Alcohol lamps.
Alcohol Bunsen burners.
Smokeless kerosene burner for heating.
Straight and looped platinum wires—mounted.
Filter paper.

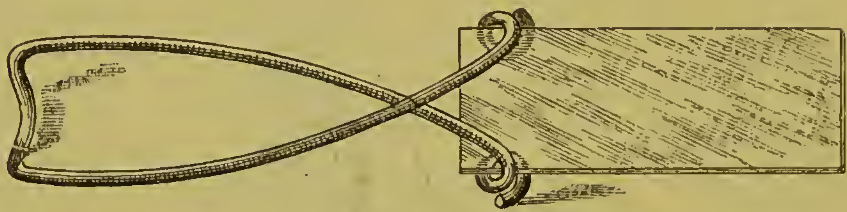


Fig. 102.—Kirkbide forceps for holding slides.

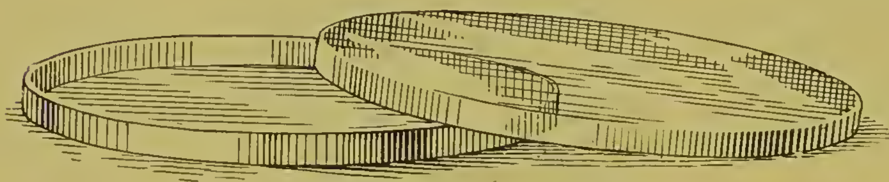


Fig. 103.—Petri dish with cover.

Wire gauze strainer for feces.
Sulphuric Acid (C. P.).
Hydrochloric Acid (C. P.).
Sodium Hydroxide (C. P.)
Absolute Alcohol.
Wood Alcohol (methyl-alcohol).
Glycerin (C. P.).
Carbolic Acid (C. P.).
Borax.
Ether.
Gelatin—best.
Neutrose.
Lactose.
Xylene.
Peptone—pure (Witte's).
Agar-Agar.

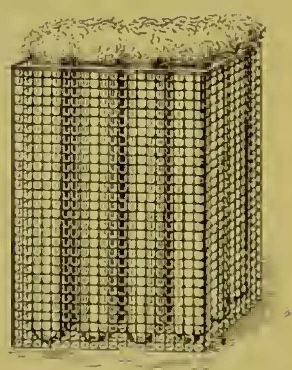


Fig. 104.—Wire basket for test-tubes.

Eosin.
Methylene blue.
Gentian violet. } Grübler's stains are generally conceded to be the best.
Fuchsin.
Tornasol blue.
Canada balsam.
Aniline oil.

For the purposes and procedures set forth in this work the foregoing list will be found to contain nearly all the necessary articles and the exercise of a little ingenuity will even permit one to dispense with a number of pieces of apparatus named, especially if ready prepared culture-media tubes and prepared stains are used, as advised.

It may, however, be desired to conduct other procedures than those described. In this case a more complete list of articles and reagents may be desired.

The following lists are from the supply tables published in the manual for the Medical Department, United States Army.

Laboratory Supplies Furnished by the Medical Department, United States Army, for Use in Permanent Army Posts and for Troops in the Field.

For Army Posts.

MICROSCOPE.

The "Continental" pattern, made by Bausch & Lomb Optical Company. *In upright cherry-wood case, with handle, lock, and extra hook and post fastenings*, the contents of which are as follows:

Stand, Universal BB . . . . . no.	1	Triple nose-piece	1
Eyepieces . . . . no.	2	*Objective*, $\frac{2}{3}$ . . . . no.	1
Abbe condenser, with iris diaphragm . . . . no.	1	*Objective*, $\frac{1}{6}$ . . . . no.	1
		Objective, $\frac{1}{12}$, *oil immersion* . . . no.	1

MICROSCOPICAL ACCESSORIES.

Articles.	Allowance for one year for posts having official population of—					
	100	200	400	600	800	1,000
Agar-agar, in 250-gm. packages . . . . . . pkgs.	1	1	1	2	2	2
Alcohol, absolute, in 250 c. c. g. s. bottle . . botts.	2	2	2	4	4	4
Aniline oil, in 50 c. c. bottle . . . . botts.	1	1	1	2	2	2
Balsam bottle . . . . no.	1	1	1	1	1	1
Bismark brown in 4-gm. bottle . . . . bott.	1	1	1	1	1	1
Canada balsam, in 30 c. c. bottle . . . . . . botts.	1	1	1	2	2	2
Cover-glass, 16 or 19 mms. square . . . . . gms.	15	15	15	30	30	30
Dropping bottle, for oil of cedar . . . . no.	1	1	1	1	1	1
Filtering paper, Swedish, Munktel's, No. 1 . quire.	1	1	1	1	1	1
Forceps, cover-glass, Stewart's pattern . . . . . no.	2	2	2	2	2	2
Forceps, small, straight, medium fine . . . . . no.	1	1	1	1	1	1
Fuchsin, in 15-gm. bottle . . . . bott.	1	1	1	1	1	1
Funnels, glass, 25 c. c. . . . . no.	2	2	2	2	2	2
Funnels, glass, 500 c. c. . . . . no.	2	2	2	2	2	2
Gelatin, in 60-gm. package . . . . pkgs.	5	5	5	10	10	10
Gentian violet, in 15-gm. bottle . . . . bott.	1	1	1	1	1	1
Methylene blue, in 15-gm. bottle . . . . . . bott.	1	1	1	1	1	1
Oil of cedar, in 30 c. c. bottle . . . . bott.	1	1	1	1	1	1
Peptone, in 250-gm. w. m. bottle . . . . . . botts.	1	1	1	2	2	2
Rods, glass, 5 mms. thick, 15, 20, and 30 cms. long, assorted . . . . gms.	200	200	300	300	500	500
Section lifter, small . . . . no.	1	1	1	1	1	1
Slides, glass, 25 x 75 mms. . . . . doz.	4	4	4	8	10	12
Stopcocks, Mohr's, for rubber tubing . . . . . . no.	2	2	2	2	2	2
Test-tubes 6 x ¾ in. . . . . gross.	2	2	2	2	2	2
Xylenum, in 250 c. c. bottle . . . . botts.	1	1	1	2	2	2

The following are supplied only on special requisition:

Microtome, Laboratary, B. and L. no.	1	*Oiler for microtome* . . . . . . no.	1
Knife for microtome . . . . . . no.	1	Hematoxylin, Merck's . . . . gms.	10
Belgian hone, 8 x 1½ in. . . . . . no.	1	Eosin . . . . gms.	10
Razor strop, Badger, Emerson's, electric, 14 in. long . . . . . no.	1	Celloidin, Schering's . . . . . gms.	50
		Staining dishes, with covers . . no.	6

BACTERIOLOGICAL SET.

One set is supplied to each post.

Baskets, wire, for sterilizer . . . no.	4
Bath, water, copper, for test-tubes no.	1
Bath, water, tripod for . . . . . no.	1
Bunsen's burner, for posts supplied with gas . . . . no.	1
Dishes, double, Petri's . . . . . no.	12
Forceps, cover-glass, Stewart's pattern . . . . no.	2
Forceps, straight, small, medium fine . . . . no.	1
Flasks, Erlenmeyer's, 250 *c. c.* . no.	6
Flasks, Erlenmeyer's, 500 *c. c.* . no.	2
Flasks, Erlenmeyer's, 1,000 *c. c.* . no.	2
Funnels, glass, 25 c. c. . . . . . . no.	4
Funnels, glass, 500 c. c. . . . . no.	2
Funnels, glass, 1,000 c. c. . . . no.	2
Incubator, lead-lined, 45.5 *x* 21.5 *x* 30.5 *cms.** . . . . no.	. .
Microburner, 1-flame . . . . . no.	1
Paper, filtering, Swedish . . . qrs.	2
Paper, litmus, blue and red, best quality, of each . . . . . sheets.	2
Pipettes, 1 c. c. . . . . no.	2
Pipettes, 5 c. c. . . . . no.	2
Platinum wire, heavy, 10-cm. pieces.	3
Platinum wire, medium, 10-cm. pieces.	6
Rubber gas tubing, ¼-in. . . . yds.	2
Regulator, gas, Reichert's, for posts supplied with gas . . . . . . no.	1
Sterilizer, hot-air, 38 *x* 28 *x* 25.5 *cm.* . . . . no.	1
Stopcocks, Mohr's, for rubber tubing . . . . no.	1
Test measures, footed, 10 c. c. . no.	1
Test-tubes, tubes, thin glass, 15 cm. by 18 mm. bore . . . . . no.	300
Thermometer, 0-50° *C.* . . . . . . no.	2
Thermometer, 0-200° *C.* . . . . no.	1

For Field Service.

MICROSCOPE. (*In cherry-wood case, with handle, lock and two keys.*)

One microscope is allowed to each field hospital.

CASE OF MICROSCOPICAL ACCESSORIES FOR FIELD SERVICE.

(*In cherry-wood case, with lock and two keys.*)

One case to each field hospital.

Alcohol and ether, w. m. bottle for, ... bott.	1
Book, memorandum, small, 3½ x 2 x ½ in. . . . . no.	1
Covers, in alcohol, w. m. bottle for, ... bott.	1
Dropper, medicine, straight . . no.	3
Envelopes, small, 1½ ins. square no.	50
Forceps, Ehrlich's . . . . . . pairs.	2
Forceps, straight, medium, fine . pair.	1
Forceps, straight, medium, heavy pair.	1
Gabbett's fluid, bottle for . . bott.	1
Glasses, cover, circles, ⅞-in., No. 1, ounce.	1
Labels for slides, ⅞-in. square . box.	1
Lamp, alcohol, ... no.	1
Loop, platinum, with handle . . no.	1
Needle case . . . . no.	1
Needle, platinum, with handle . no.	1
Needle, bayonet-pointed, 2 *ins. long* . . . . no.	3
Pencil, glass, blue wax, Faber's no.	1
Pencil, lead . . . . no.	1
Slides, glass, 3 x 1 in. . . . . . gross.	¼
Slides, in alcohol, w. m. bottle for, ... bott.	1
Stain, carbol-fuchsin, bottle for bott.	1
Stain, methylene blue, bottle for, bott.	1

*At stations where there is no gas, an incubator, to be heated by petroleum flame, may be obtained upon application.

Gram's iodine solution
- Iodine, ... 1 gram.
- Iodide of potassium, 2 grams.
- Water, ... 300 c. c.

is used in connection with gentian violet. Exposure to the violet stain is followed by exposure to the iodine solution and then to alcohol.

The method, known as *Gram's method*, is as follows:

Stain the fixed bacterial preparation (cover glass) with an anilin-water-gentian-violet solution for two minutes. Then expose to the iodine-potassium-iodide solution for a minute and a half. Then wash in alcohol as long as the violet color comes away. Wash in water, dry and examine.

Some bacteria retain a violet stain and others are entirely decolorized. This response to Gram's method—either positive or negative—is a recognized means of identifying certain important bacteria.

Löffler's methylene blue, a much used bacterial stain, is made as follows:
- Concentrated alcoholic solution of methylene blue, ... 30 c. c.
- Watery solution (1:10,000) of caustic potash (potassium hydrate), ... 100 c. c.

Anilin oil, used when intense stains are desired, is added to distilled water; 5 parts of oil to 100 of water, well shaken and filtered. When clear it may be used with alcoholic solutions of fuchsin, methylene blue and gentian violet, taking 100 c. c. of anilin-water, and 10 c. c. each of alcohol and an alcoholic solution of the dye.

To make *Nutrient Bouillon* proceed as follows: Dissolve 3 grams of beef extract (Armour's or Liebig's), 10 grams of *pure* peptone (Witte's), and 5 grams of table salt (sodium chloride) in a liter of water. Boil for ten minutes and render neutral or faintly alkaline by adding, drop by drop, sodium hydroxide solution, testing meanwhile with litmus paper. Now filter into clean sterile test-tubes or flasks (using filter paper), cork with non-absorbent cotton, and sterilize for half an hour in the steam sterilizer for three consecutive days. If precipitates form the bouillon is probably too alkaline. Correct by adding, drop by drop, weak hydrochloric acid, testing meanwhile with litmus. Re-sterilize after adding the acid solution. The peptone *must be pure*.

To make *Nutrient Agar-agar*, a vegetable gelatin medium, not quite transparent and with a higher melting point than gelatin, proceed as follows: Cut up 10 grams of agar into fine pieces and dissolve in a small amount of water over a burner. Dissolve 3 grams of beef extract, 10 grams of *pure* peptone and 5 grams of sodium chloride in a liter of water. Now add the

dissolved agar and boil for two hours, skimming frequently. Before adding the agar it will be well to neutralize the solution of beef extract, peptone and salt. The agar solution will be slightly alkaline in reaction. Weak hydrochloric acid, drop by drop, may be used to overcome alkalinity and sodium hydroxide solution to overcome acidity. Boiling should reduce the amount to 1 liter. After boiling for the required time remove and cool to 60° C. Then stir into the solution the whites of two eggs, beaten up with a little water, which will coagulate and entangle the particles of solid matter in the medium. Now boil again for a few minutes. Filter, while hot, through cotton, filter paper or gauze, into clean, sterile test-tubes or flasks. These should then be plugged with sterile nonabsorbent cotton and sterilized upon three successive days for thirty minutes each day.

To make *Glycerin Agar* proceed as above but add six percent of pure glycerin before sterilizing.

For dextrose or lactose agar—add one percent of dextrose or lactose before sterilizing.

To make *Nutrient Gelatin Medium* proceed as directed for nutrient agar, substituting 150 grams of the best gelatin for the 10 grams of agar (100 grams of gelatin will do outside the tropics). Boil for ten minutes only. If cloudy, melt and refilter, making sure that the reaction is not too alkaline. Beef extract, 3 grams; *pure* peptone, 10 grams; sodium chloride, 5 grams; best gelatin, 150 grams; water, 1 liter.

To make *slant tubes* of either gelatin or agar, let the tubes cool in a leaning position, when the solidified medium will present a slanting surface.

Agate or enamel-ware vessels should be used for boiling the various media —which should be carefully stirred, at the bottom only, to prevent burning, after the whites of eggs are added for clearing.

Plate Culture Media may be prepared by melting the test-tubes of agar or gelatin media and pouring into sterile Petri dishes. The inoculation of this medium, however, with the material under investigation (pus, blood, vomitus, urine, feces, etc.), is made while the melted medium is in the test-tubes. Inoculate with a platinum loop, flame sterilized, and dipped first into the material to be investigated and then into the test-tube of melted medium, using one or several loopfuls of the material under investigation. The tube is then corked and agitated without wetting the cotton stopper, and from this inoculated tube several loopfuls of medium may be transferred to other tubes—and so on—increasing the dilution greatly with each transplanting. The inoculated tubes of liquid medium are now poured into sterile Petri

dishes, covered and labeled. The medium soon hardens and in due time colonies appear in it.

Inoculations may also be made directly to plate media by puncture or streaking the surfaces with the platinum loop or wire.

In examining these colonies a hand lens may be used or the Petri dish may be placed under the low-power objective upon the stage of the microscope.

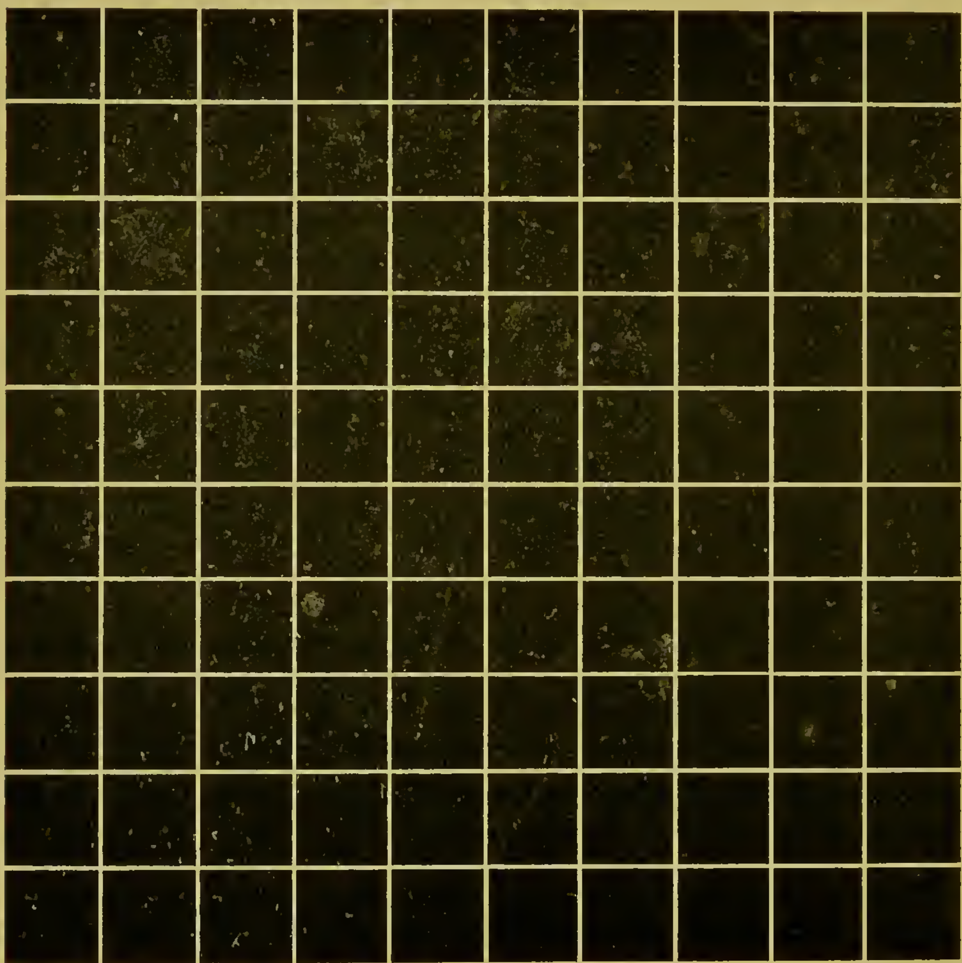


Fig. 105.—Surface divided in square centimeters for counting colonies. May be placed under Petri dish.

Essential precautions include the *invariable flaming* of the platinum loop and the lips and necks of test-tubes and flasks, and the handling of the sterile Petri dishes with sterilized forceps only. The fingers should never be carried to the lips or mouth while working in the laboratory with pathologic material or cultures.

To prepare *Potato* as a *Culture Medium*, cut off both ends of a thoroughly scrubbed, boiled or steamed potato, and with a cork borer, fruit corer, trephine or similar implement, cut cylinders of potato and then divide each cylinder diagonally into two slant-surfaced pieces. These may be placed in test-tubes, a small amount of water being placed in the

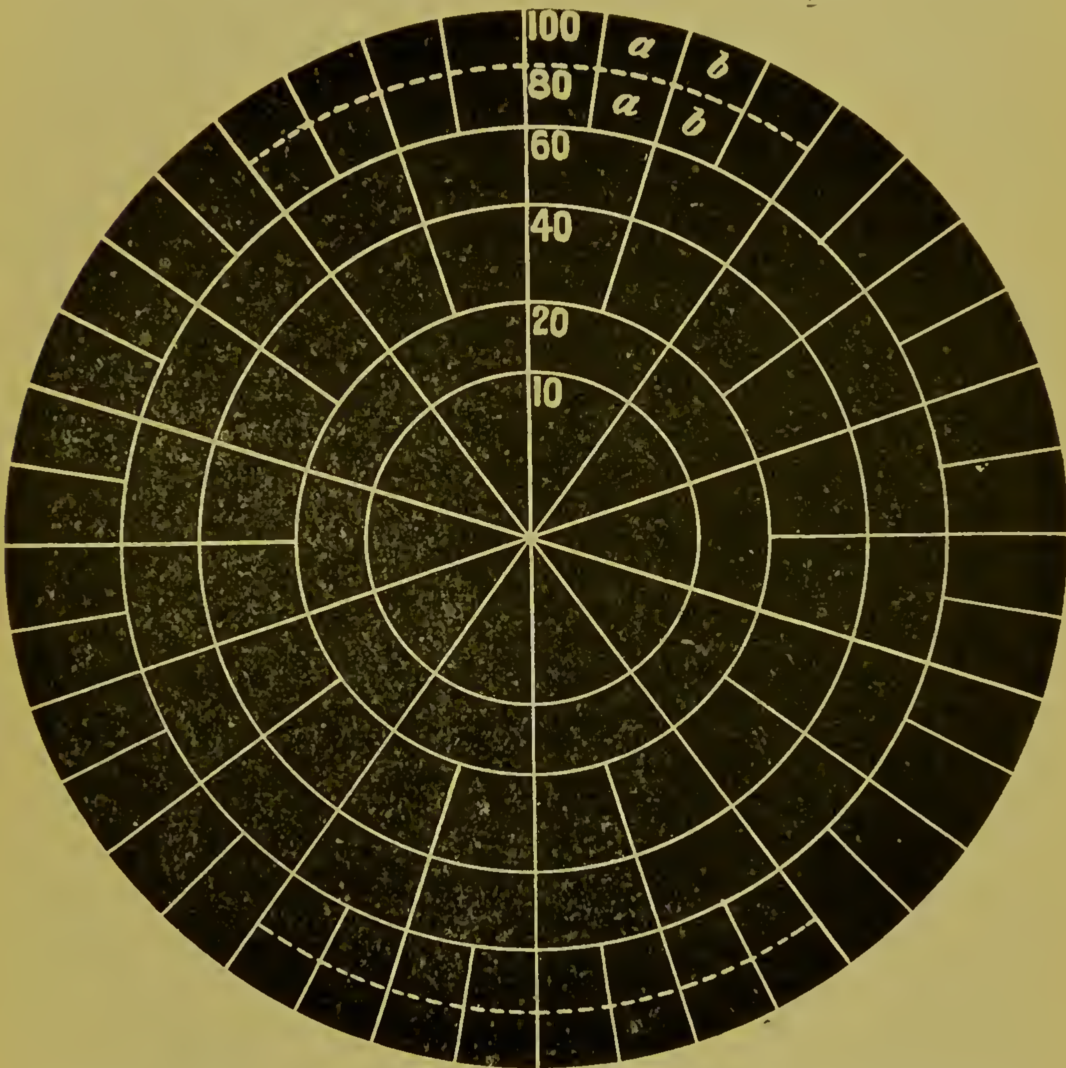


Fig. 106.—Plate for counting colonies of bacteria in Petri dishes. Place under the dish.

bottom of the tubes to keep the potato moist. To prevent the potato cylinder from slipping to the bottom of the tube, place a small amount of nonabsorbent cotton in the bottom to support the cylinder. Plug the tube with nonabsorbent cotton. These tubes should be frequently prepared and steam sterilized for a long time and upon repeated days, to destroy the resistant spores of the potato bacillus.

The foregoing brief directions for preparing media are not intended to take the place of more elaborate and explicit instructions to be found in works upon pathology and bacteriology—as for example the excellent works of Coplin (Pathology) and Williams (Manual of Bacteriology). They are believed, however, to be sufficiently complete to guide the clinical worker possessed of moderate ingenuity, limited appliances, and some grounding in the fundamentals of bacteriology, when used in connection with the methods of "laboratory detection" detailed at the close of the various chapters in this book.

CONVERTIBLE TEMPERATURE TABLES.

To convert Fahrenheit degrees to Centigrade, if above zero, subtract 32, multiply by 5, and divide by 9. Above zero, $C^\circ = F^\circ - 32 \times \frac{5}{9}$.

To convert Centigrade degrees to Fahrenheit, if above zero, multiply by 9, divide by 5, and add 32. Above zero, $F^\circ = C^\circ \times \frac{9}{5} + 32^\circ$.

Centigrade°	Fahrenheit°		Centigrade°	Fahrenheit°	
100	212	*Water Boils.*	15	59	
72	161.6		10	50	
60	140		5	41	
55	131		1	33.8	
50	122		Zero	32	*Water Freezes.*
45	113		—5	23	
43	109.4		—10	14	
42	107.6		—15	5	
41	105.8		—17	1.4	
40	104			—Zero	
39	102.2	Human Body Temperature.	—20	—4	
38	100.4		—25	—13	
37	98.6	Normal Body Heat.	—30	—22	
36	96.8		—35	—31	
35	95		—40	—40	
30	86		—45	—49	
25	77		—49	—56.2	
20	68				

EQUIVALENTS OF WEIGHTS AND MEASURES, CUSTOMARY AND METRIC.

From Potter's Materia Medica, Pharmacy and Therapeutics.

Troy Weight. Grains.	Metric Weight and Measure. Gr.] [Cc.	Fluid Measure. Minims	Troy Weight. Oz.	Troy Weight. Grains.	Metric Weight and Measure. Gr.] [Cc.	Fluid Measure. Oz.	Fluid Measure. Minims.
1-640	.0001	....		60 [1ʒ	3.888		63.1
1-320	.0002	....		61.7	4		64.9
1-200	.0003	....		77.2	5		81.1
1-160	.0004	....		80	5.184		84.1
1-128	.0005	....		92.6	6		97.4
1-100	.0006	....		95.1	6.161		100
1-64	.001 Mg.	....		100	6.480		105.2
1-50	.0013	....		108	7		113.6
1-40	.0016	....		109.37 [¼ av.oz.	7.088		115.9
1-30	.002	....		114.1	7.393		120 [2ʒ
1-20	.003	....		120 [2ʒ	7.775		126.2
1-16	.004	....		123.5	8		129.8
1-12	.005	....		138.9	9		146.1
1-10	.006	....		142.6	9.241		150
1-8	.008	....		150	9.719		157.8
1-6	.010	....		154.3	10		162.3
1-4	.016	....		170	11		178.5
1-3	.020	....		171.1	11.090		180 [3ʒ
1-2	.032	....		180 [3ʒ	11.663		189.3
5-8	.040	....		185.2	12		194.8
3-4	.049	....		200.6	13		211
4-5	.050	....		210	13.607		220.9
9-10	.060	....		216.1	14		227.2
.95	.062	1		218.75 [½ av.oz.	14.175		230.1
1	.065	1.05		228.2	14.786		240 [4ʒ
1.5	.097	1.7		231.5	15		243.4
2	.130	2.1		240 [4ʒ	15.551		252.4
2.9	.185	3		246.9	16		259.7
3	.194	3.2		262.3	17		275.9
3.8	.246	4		277.8	18		292.1
4	.259	4.2		285.2	18.483		300 [5ʒ
4.8	.300	5		293.2	19		308.4
5	.324	5.3		300 [5ʒ	19.440		315.5
5.7	.370	6		308.6	20		324.6
6	.389	6.3		324.1	21		340.8
6.7	.431	7		339.5	22		357.1
7	.454	7.4		342.3	22.180		360 [6ʒ
7.7	.500	8.1		354.9	23		373.3
8	.518	8.4		360 [6ʒ	23.327		378.6
8.6	.554	9		370.4	24		389.5
9	.583	9.5		380.3	24.644		400
9.5	.616	10		385.8	25		405.7
10	.648	10.5		390	25.271		410.2
11	.713	11.6		399.3	25.870		420 [7ʒ
12	.775	12.6		401.2	26		422
12.4	.801	13		416.7	27		438.2
13	.842	13.7		420 [7ʒ	27.214		441.7
14	.907	14.7		432.1	28		454.4
14.3	.924	15		437.5 [1 av.oz.	28.350		460.1
15	.972	15.9		447.5	29		470.7
15.432	1	16.23		456.4	29.574	1	.... [1℥
19	1.232	20		463	30	1	6.9
20	1.296	21		478.4	31	1	23.1
23.8	1.540	25	1	.... [1℥	31.103	1	24.8
28.5	1.848	30 [½ʒ	1	137.3	40	1	169.2
30 [½ʒ	1.944	31.6	1	291.6	50	1	331.5
30.9	2	32.5	1	432.8	59.147	2	....
38	2.464	40	1	445.9	60	2	13.8
40	2.592	42.1	2	....	62.207	2	49.7
42.8	2.772	45	2	409.2	88.721	3	....
46.3	3	48.7	3	....	93.310	3	74.5
47.5	3.080	50	3	103.2	100	3	183.1
50	3.240	52.6	4	362	147.869	5	....
54.69 [⅛ av.oz.	3.544	57.5	5	....	155.517	5	124.1
57	3.696	60 [1ʒ	32	72.4	1000	33	390.6

LITERATURE.

Alden, Col. C. H.: Trans. American Climatolog. Assoc., 1901.

Allyn and Behrend: Amer. Medicine, July, 1901.

American Medicine Editorials, 1903, 1904, 1905.

Anders: Practice of Medicine.

Annual Reports of Surgeon-General, United States Army, 1899, 1900, 1901, 1902, 1903, 1904, 1905.

Ashford and King: New Orleans Med. and Surgical Jour., April, 1904.

Ashford: N. Y. Med. Journal, p. 552, 1901.

Banister, Maj. J. M.: Report Surgeon-General, 1904.

Begg, Chas.: Journal Royal Army Med. Corps, July, 1905.

Blumer: Journal American Med. Assoc., July 15, 1905.

Boycott: London letter Journal A. M. Assoc., July 9, 1905.

Bondurant: New York Med. Journal, Vol. 78, p. 8, 1903.

Braun: Animal Parasites of Man.

Bulletin Number 5, Biolog. Lab. Dept. Interior of United States.

Butler: Diagnostics of Internal Medicine.

Calvert, Lt.: Report Surgeon-General United States Army, 1900.

Carrol, Lt. Jas.: Annual Reports of Surgeon-General, United States Army, and Transaction of American Society of Tropical Medicine, 1905.

Castellani: British Med. Journal, May 23, 1903. Proceedings Royal Society, May, 8, 1903; Journal Tropical Med., June 1 and Aug. 1, 1903; Jan. 1, 1906.

Christophers: The Practical Study of Malaria, 1905.

Circular Number 3, Board for Investigating Tropical Diseases, Manila, 1901.

Clayton, F. H.: Journal Trop. Med., Jan. 2, 1905.

Clegg: Bulletin No. 5. Bio. Lab. Dept. Int., 1903.

Cohen: System of Physiological Therapeutics.

Coplin: Pathology.

Craig, Lt. Chas. F.: Annual Reports of Surgeon-General, United States Army. Estivo-autumnal Fevers. American Jour. Med. Sciences, Vol. 126, p. 798, 1903; Internat. Clinics, 1904.

Curry, J. G.: Boston Med. and Surg. Jour., March 21, 1901. Annual Reports of Surgeon-General, United States Army.

DaCosta, J. M.: Medical Diagnosis.

DaCosta, J. C., Jr.: Clinical Hematology.

Daniels: Laboratory Studies in Trop. Medicine.

Dantec, A. Le.: Pathologie Exotique, Paris, 1905.

Danysz, J.: British Med. Jour., April 23, 1904.

Editorials, Journal Amer. Med. Assoc., July 30, 1904; Aug. 26, 1905; Sept. 23, 1905.

Gazette Med. Belge., 1904.

Fearnsides: Journal of Economic Biology, 1906, Vol. 1, Part II.

Gerrard: Beriberi, An Essay, London, 1904.

Giles: Climate and Health in Hot Countries.

Girard, Col. A. C.: Reports of Surgeon-General, United States Army.

Gould and Pyle: Cyclopedia of Medicine and Surgery.

Gunn: California State Jour. of Med., Vol. 3, p. 128, 1905.

Guiteras: American Medicine, Vol. 4, p. 100, 1902.

Hare: Practice of Medicine, 1905.

Harris: Prize Essay, College of Physicians, Phila., 1901.

Horrocks, W. H.: Jour. Royal Army Med. Corps, pp. 311, 343, 1906.

Howard, L. O.: Notes on Mosquitos of the U. S. Bulletin 25, Dept. Agric.

Inouye, Z.: Archiv. f. Verdauungs Krankheiten, 1905.

International Medical Annual, 1894

International Clinics, Vols. II and IV, 1904.

Jackson, T. W.: Phila. Med. Journal, Apr. 5, Apr. 19, 1902. Annual Reports Surgeon-General, United States Army, 1900, 1901, 1902.

Jarvis, C.: Paris. Internat. Clinics, Vol. II., 1904.

Journal of Tropical Medicine, 1904, 1905, 1906.

Journal of Royal Army Med. Corps, 1904, 1905, 1906.

King: American Med., Vol. 6, p. 391, 1903. New Orleans Med. and Surg. Jour., 1904.

Koch, Robert: Deut. Med. Wochenschrift, 1904.

Kolle: Modern Clinical Medicine, 1905.

Leonard: Jr. Amer. Med. Assoc., Aug. 26, 1905.

Liston: Indian Medical Gazette, Feb. 1905.

Loos: Centralb. f. Bakteriol. u. Parasitenk, May, 1901.

Lynch, Maj. Chas.: Annual Rept. Surgeon-Gen., United States Army, 1902.

Mabrey and Gemmill: Jr. Am. Med. Assoc., Dec. 20, 1902.

Manouvriez: Bulletin d. l'Académie de Medicin, Paris, Year 48, No. 23.

Manson, Sir Patrick: Tropical Diseases, 1904. Lane Lectures, 1905.

Mason, Maj. Chas.: Internat. Clinics, Vol. 2, 1904.

Mercier, A.: Le Paludisme, Paris, 1905.

Musgrave: Reports Surgeon-General, United States Army. Bulletin, No. 5, Bio. Lab. Dep't. Int. U. S., 1903.

McCrea: Internat. Clinics, Vol. 2, 1904.

McCaw, Major W.: Report Surgeon-General, United States Army, 1904.

McNeal: Journal Infectious Diseases, 1904.

Neumann: Deutsche Med. Wochenschrift, 1904.

Nichols: Medical News, Vol. 84, p. 785, 1904.

Nicholson and Rankin: Medical News, Feb. 19, 1904.

Norsa: Riforma Medica, 1904.

Novy: Journal Infectious Diseases, 1904.

Osler, Wm.: Practice of Medicine.

Pernet, G.: The Differential Diagnosis of Syphilitic and Non-Syphilitic Affections of the Skin.

Reed, Major Walter: Reports of the Surgeon-General, United States Army.

Report of Wellcome Research Laboratories at Khartoum, 1906.

Ross: Mosquito Brigades.

Salazar: Jour. Assoc. Mil. Surgeons, March, 1905.

Sandwith: Medical Diseases of Egypt. Part I, 1905.

Schaefer: Medical News, Vol. 79, p. 655, 1901.

Schamberg: Diseases of the Skin.

Schaudinn: Arbeiten aus der Kais. Gesundheitsamte, Vol. XX, 1904.

Scheube: Diseases of Warm Countries.

Shakespeare: Report of Cholera in India and Europe, 1890.

Shipley: Jour. of Economic Biology, Vol. 1., Part II., 1900.

Simpson: Treatise on Plague. Report on Plague in Hong-kong. Maintenance of Health in the Tropics, 1905.

Smith, A. J.: In Tyson's Practice of Medicine (Parasites). Internat. Clinics, Vol. 2, 1904.

Smith, C. A.: Jour. Amer. Med. Assoc., Vol. 41, p. 709, 1903. Vol. 43, p. 592, 1904; Oct. 18, 1905.

Sternberg: Infection and Immunity, 1903.

Stiles: Amer. Medicine, Vol. 3, p. 777, 1902. Bulletin No. X., P. H. and M. H. S., 1903. Brooklyn Med. Journal, Vol. 17, p. 51, 1903. Buffalo Med. Jour., Vol. 42, p. 517, 1903. Journal Amer. Med. Assoc., Vol. 41, p. 171, 1903.

Strong, Lt. R. P.: Annual Reports Surgeon-General, United States Army, and Bulletins of Tropical Diseases (Govt. prints, Manila).

Sutton: Jour. Amer. Med. Assoc., Dec. 17, 1904.

Tetamore, F. L.: Report of Surgeon General, United States Army, 1901. Transactions of the Pan-American Medical Congress. Transactions of the American Society of Tropical Medicine, 1905.

Tyson, James: Practice of Medicine, 1905.

Wainwright: Medical News, Vol. 84, p. 785, 1904.

Wellman, F. C.: N. Y. Med. Jour., and Phila. Med. Jour., Aug. 12, 19,

26; Sept. 2, 1905. Jour. Trop. Med., Oct. 2, 1905. American Medicine July 22, 1905.

Williams: Manual of Bacteriology, 1903.

Wilson. J. C.: Modern Clinical Medicine, 1905.

Woodruff, Maj. Chas.: Effects of Tropical Light on White Men.

Wright, Hamilton: Studies from Institute for Medical Research. Federated Malay States, Vol. 2, Nos. 1 and 2, 1902, 1903.

INDEX.